General

Guideline Title

Tuberculosis.

Bibliographic Source(s)

National Institute for Health and Care Excellence (NICE). Tuberculosis. London (UK): National Institute for Health and Care Excellence (NICE); 2016 Jan 13. 177 p. (NICE guideline; no. 33).

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: National Collaborating Centre for Chronic Conditions. Tuberculosis. Clinical diagnosis and management of tuberculosis, and measures for its prevention and control. London (UK): National Institute for Health and Clinical Excellence (NICE); 2011 Mar. 64 p. (Clinical guideline; no. 117).

This guideline meets NGC's 2013 (revised) inclusion criteria.

Regulatory Alert

FDA Warning/Regulatory Alert

Note from the National Guideline Clearinghouse: This guideline references a drug(s) for which important revised regulatory and/or warning information has been released.

- August 31, 2016 – Opioid pain and cough medicines combined with benzodiazepines : A U.S. Food and Drug Administration (FDA) review has found that the growing combined used of opioid medicines with benzodiazepines or other drugs that depress the central nervous system (CNS) has resulted in serious side effects, including slowed or difficult breathing and deaths. FDA is adding Boxed Warnings to the drug labeling of prescription opioid pain and prescription opioid cough medicines and benzodiazepines.
- March 22, 2016 – Opioid pain medicines : The U.S. Food and Drug Administration (FDA) is warning about several safety issues with the entire class of opioid pain medicines. These safety risks are potentially harmful interactions with numerous other medications, problems with the adrenal glands, and decreased sex hormone levels. They are requiring changes to the labels of all opioid drugs to warn about these risks.

Recommendations

Major Recommendations

Note from the National Guideline Clearinghouse (NGC): This guideline was developed by the Internal Clinical Guidelines Team on behalf of the National Institute for Health and Care Excellence (NICE). See the "Availability of Companion Documents" field for the full version of this guidance and related appendices.

Note from NGC and NICE: In May 2016, NICE clarified the recommendations regarding diagnosing latent tuberculosis in adults in order reflect the sequencing of tests. In addition, references to interferon-gamma release assay (IGRA) status were removed. The recommendations below reflect these changes.

Recommendations are marked as:

- [new 2016] if the evidence has been reviewed and the recommendation has been added or updated
- [2016] if the evidence has been reviewed but no change has been made to the recommended action
- [2006] if the evidence has not been reviewed since 2006
- [2006, amended 2011] or [2011] if the evidence has not been reviewed since 2006
- [2012] if the evidence has not been reviewed since 2012
- [2006, amended 2011, amended 2016] or [2011, amended 2016] if the evidence has not been reviewed since 2011, but either changes have been made to the recommendation wording that change the meaning or NICE has made editorial changes to the original wording to clarify the action to be taken (see below).
- [2006, 2012, amended 2016] or [2012, amended 2016] if the evidence has not been reviewed since 2012, but either changes have been made to the recommendation wording that change the meaning or NICE has made editorial changes to the original wording to clarify the action to be taken.

Some recommendations are made with more certainty than others. The wording of the recommendations reflects this. For example, the Guideline Development Group (GDG) uses 'offer' to reflect a strong recommendation, usually where there is clear evidence of benefit. The GDG uses 'consider' to reflect a recommendation for which the evidence of benefit is less certain. The strength of recommendation is defined at the end of the "Major Recommendations" field.

Preventing Tuberculosis (TB)

Raising and Sustaining Awareness of TB

Among Health Professionals and Those Working with High-Risk Groups

Multidisciplinary TB teams (in collaboration with Public Health England, primary care, the voluntary sector and Health Education England) should identify and support an ongoing TB education programme for local professionals in contact with the general public, and at-risk groups in particular. This includes, for example, staff in emergency departments, general practitioners (GPs) and wider primary care staff, people who work in housing support services, staff who support migrants and those working in walk-in centres, hostels, substance misuse projects and prisons. [2012, amended 2016]

Multidisciplinary TB teams should ensure the education programme increases other professionals' awareness of the possibility of TB and reduces the stigma associated with it. The programme should include detail on:

- Causes of TB, how it is transmitted, and the signs and symptoms
- Lifestyle factors that may mask symptoms
- Local epidemiology, highlighting under-served groups, other high-risk groups and the fact that TB also occurs in people without risk factors
- Principles of TB control:
    - Early diagnosis and active case-finding
    - How to support treatment (including directly observed therapy)
    - Drug resistance
    - Awareness of drug interactions (including factors such as effect on contraception efficacy)
    - Contact investigation after diagnosing an active case
    - The importance of adhering to treatment
    - Treatment for TB is free for everyone (irrespective of eligibility for other National Health Service [NHS] care)
    - Social and cultural barriers to accessing health services (for example, fear of stigma and staff attitudes)
    - Local referral pathways, including details of who to refer and how
    - The role of allied professionals in awareness-raising, identifying cases and helping people complete treatment

- Misinformation that causes fear about TB, including concerns about housing people with the condition
- The best ways to effectively communicate all the above topics with different groups [2012, amended 2016]

Statutory, community and voluntary organisations and advocates working with the general public, and under-served and high-risk groups in particular, should share information on TB education and awareness training with all frontline staff. (They should get information on this from the local multidisciplinary TB team.) [2012, amended 2016]

If possible, statutory, community and voluntary organisations should ensure peers from under-served groups and anyone else with experience of TB contribute to, or lead, awareness-raising activities. (Peers who lead such activities will need training and support.) [2012, amended 2016]

Among High-Risk Groups

Multidisciplinary TB teams should help professionals working in relevant statutory, community and voluntary organisations to raise awareness of TB among under-served and other high-risk groups. These professionals should be able to explain that treatment for TB is free and confidential for everyone (irrespective of eligibility for other NHS care). They should also be able to provide people with details of:

- How to recognise symptoms in adults and children
- How people get TB
- The benefits of diagnosis and treatment (including the fact that TB is treatable and curable)
- Location and opening hours of testing services
- Referral pathways, including self-referral
- The potential interaction of TB medication with other drugs, for example, oral contraceptives and opioids (especially methadone) and human immunodeficiency virus (HIV) treatment
- TB/HIV co-infection
- How to address the myths about TB infection and treatment (for example, to counter the belief that TB is hereditary)
- How to address the stigma associated with TB
- The risk of migrants from high-incidence countries developing active TB – even if they have already screened negative for it
- Contact tracing [2012, amended 2016]

Multidisciplinary TB teams and others working with at-risk groups should use high-quality material to raise awareness of TB (see section below). [2012, amended 2016]

Multidisciplinary TB teams and others working with the general public, and with under-served and other high-risk groups in particular, should include information on TB with other health-related messages and existing health promotion programmes tailored to the target group. [2012, amended 2016]

Multidisciplinary TB teams should work in partnership with voluntary organisations and 'community champions' to increase awareness of TB, in particular among under-served groups at risk of infection but also in the general population. If possible, peers who have experience of TB should contribute to awareness-raising activities and support people in treatment. [2012, amended 2016]

Providing Information for the Public about TB

National organisations (for example, National Knowledge Service – Tuberculosis, TB Alert, Public Health England, Department of Health and NHS Choices) should work together to develop generic, quality-assured template materials with consistent up-to-date messages. These materials should be made freely available and designed so that they can be adapted to local needs. [new 2016]

Multidisciplinary TB teams should use these templates for general awareness raising and targeted activities in under-served and other high-risk groups. Involve the target group in developing and piloting the materials. [new 2016]

The content of any materials should:

- Be up-to-date and attractively designed, including pictures and colour if possible
- Be culturally appropriate, taking into account the language, actions, customs, beliefs and values of the group they are aimed at
- Be tailored to the target population's needs
- Include risks and benefits of treatment, and how to access services, advice and support
- Dispel myths
- Show that, by deciding to be tested and treated for TB, a person can be empowered to take responsibility for their own health
- Use language that encourages the person to believe that they can change their behaviour
- Be simple and succinct [new 2016]

Make the material available in a range of formats such as written, braille, text messages, electronic, audio (including podcasts), pictorial and video. Make them freely available in a variety of ways, for example, online, as print materials or on memory sticks. [new 2016]

Disseminate materials in ways likely to reach target groups, for example, via culturally specific radio or TV stations, at shelters, and at community, commercial or religious venues that target groups attend regularly. [new 2016]

Bacille Calmette-Guerin (BCG) Vaccination

To improve the uptake of BCG vaccination, identify eligible groups (in line with the Department of Health's Green Book) opportunistically through several routes, for example:

- New registrations in primary care and with antenatal services, or other points of contact with secondary or tertiary care
- People entering education, including university
- Links with statutory and voluntary groups working with new entrants and looked-after children and young people
- During contact investigations [new 2016]

When BCG vaccination is being recommended, discuss the benefits and risks of vaccination or remaining unvaccinated with the person (or, if a child, with the parents), so that they can make an informed decision. Tailor this discussion to the person, use appropriate language, and take into account cultural sensitivities and stigma. [2006]

If people identified for BCG vaccination through occupational health, contact tracing or new entrant screening are also considered to be at increased risk of being HIV-positive, offer them HIV testing before BCG vaccination. [2006]

BCG Vaccination in Neonates (0–4 weeks)

Identify babies eligible for vaccination (in line with the Green Book) before birth, ideally through antenatal services. [new 2016]

Discuss neonatal BCG vaccination for any baby at increased risk of TB with the parents or legal guardian. [2006]

Preferably vaccinate babies at increased risk of TB before discharge from hospital or before handover from midwifery to primary care. Otherwise, vaccinate as soon as possible afterwards, for example, at the 6-week postnatal check. [new 2016]

Incorporate computer reminders into maternity service (obstetrics) IT systems for staff, to identify and offer BCG vaccination to babies eligible for vaccination. [new 2016]

Provide education and training for postnatal ward staff, midwives, health visitors and other clinicians on identifying babies eligible for vaccination, local service information and providing BCG vaccination, including:

- Case definition for at-risk groups to be offered vaccination
- Information about the local BCG vaccination policy that can be given verbally, in writing or in any other appropriate format (see sections above) to parents and carers at the routine examination of the baby before discharge
- Local service information about BCG vaccination, such as pre-discharge availability of neonatal vaccination, local BCG clinics and referral for BCG vaccination if this is not available in maternity services
- Administration of BCG vaccination and contraindications [new 2016]

Primary care organisations with a high incidence of TB should consider vaccinating all neonates soon after birth. [2006]

In areas with a low incidence of TB (see Public Health England's TB rate bands, published in their Annual Report), primary care organisations should offer BCG vaccination to selected neonates who:

- Were born in an area with a high incidence of TB or
- Have 1 or more parents or grandparents who were born in a high-incidence country or
- Have a family history of TB in the past 5 years [2006, amended 2016]

BCG Vaccination for Infants (0–5 years) and Older Children (6–15 years)

Routine BCG vaccination is not recommended for children aged 10 to 14 years.

- Healthcare professionals should opportunistically identify unvaccinated children older than 4 weeks and younger than 16 years at increased risk of TB who would have qualified for neonatal BCG (see recommendation above) and provide Mantoux testing[1] (see section below) and BCG vaccination (if Mantoux-negative).

- This opportunistic vaccination should be in line with the Green Book. [2006, amended 2016]

Mantoux testing should not be done routinely before BCG vaccination in children younger than 6 years unless they have a history of residence or prolonged stay (more than 1 month) in a country with a high incidence of TB. [2006]

BCG Vaccination for New Entrants from High-Incidence Areas

Offer BCG vaccination to new entrants who are Mantoux-negative who:

- Are from high-incidence countries and
- Are previously unvaccinated (that is, without adequate documentation or a BCG scar) and
- Are aged:
    - Younger than 16 years or
    - 16–35 years from sub-Saharan Africa or a country with a TB incidence of 500 per 100,000 or more [2006, amended 2016]

Encouraging Uptake among Infants, Older Children and New Entrants

Deliver the following interventions in primary care settings to improve uptake of BCG vaccination in people from eligible groups (as outlined in the Green Book):

- Education and support for practice staff, including:
    - Raising awareness of relevant guidelines and case definition for at-risk groups
    - Promoting BCG and TB testing in eligible groups
- Incorporating reminders for staff (prompts about eligibility for BCG) on practice computers (for example, embedded in medical records)
- Consider financial incentives for practices for identifying eligible groups for BCG and TB testing
- Reminders ('immunisations due') and recall ('immunisations overdue') for people who are eligible for vaccination or for parents of infants and children who are eligible, as outlined in the Green Book. (This could include written reminders, telephone calls from a member of staff or a computerised auto dialler, text messages or a combination of these approaches.) [new 2016]

Use home visits to give information and advice to people who are disadvantaged on the importance of immunisation. This should be delivered by trained lay health workers, community-based healthcare staff or nurses. [new 2016]

BCG Vaccination for Healthcare Workers

Offer BCG vaccination to healthcare workers and other NHS employees who have contact with patients or clinical specimens, irrespective of age, who:

- Are previously unvaccinated (that is, without adequate documentation or a BCG scar) and
- Are Mantoux-negative (see "Diagnosing Latent TB in Adults" below) [2006, amended 2016]

BCG Vaccination for Contacts of People with Active TB

Offer BCG vaccination to Mantoux-negative contacts of people with pulmonary and laryngeal TB (see "Diagnosing Latent TB in All Age Groups" below) if they:

- Have not been vaccinated previously (that is, there is no adequate documentation or a BCG scar) and
- Are aged 35 years or younger or
- Are aged 36 years and older and a healthcare or laboratory worker who has contact with patients or clinical materials [2006, amended 2016]

BCG Vaccination for Other Groups

Offer BCG vaccination to previously unvaccinated, Mantoux-negative people aged 35 years or younger in the following groups at increased risk of exposure to TB, in accordance with the Green Book:

- Veterinary and other staff such as abattoir workers who handle animal species known to be susceptible to TB, such as simians
- Prison staff working directly with prisoners
- Staff of care homes for older people
- Staff of hostels for people who are homeless and facilities accommodating refugees and asylum seekers
- People going to live or work with local people for more than 3 months in a high-incidence country [2006, amended 2016]

Preventing Infection in Specific Settings

Healthcare Environments: New NHS Employees

Employees new to the NHS who will be working with patients or clinical specimens should not start work until they have completed a TB screen or health check, or documentary evidence is provided of such screening having taken place within the preceding 12 months. [2006]

Employees new to the NHS who will not have contact with patients or clinical specimens should not start work if they have signs or symptoms of TB. [2006]

Health checks for employees new to the NHS who will have contact with patients or clinical materials should include:

- Assessment of personal or family history of TB
- Asking about symptoms and signs, possibly by questionnaire
- Documentary evidence of TB skin (or interferon-gamma release assay) testing within the past 5 years and/or BCG scar check by an occupational health professional, not relying on the applicant's personal assessment [2006]

See recommendations below under "Diagnosing Latent TB in Adults" for screening new NHS employees for latent TB. [2006, amended 2011]

Employees who will be working with patients or clinical specimens and who are Mantoux- or interferon-gamma release assay-negative (see "Diagnosing Latent TB in Adults" below) should have an individual risk assessment for HIV infection before BCG vaccination is given. [2006, amended 2016]

Offer BCG vaccination to employees of any age who are new to the NHS and are from countries of high TB incidence, or who have had contact with patients in settings with a high TB prevalence, and who are Mantoux-negative. [2006, amended 2011]

If a new employee from the UK or other low-incidence setting, who has not had a BCG vaccination, has a positive Mantoux test and a positive interferon-gamma release assay, they should have a medical assessment and a chest X-ray. They should be referred to a TB clinic to determine whether they need TB treatment if the chest X-ray is abnormal, or to determine whether they need treatment of latent TB infection if the chest X-ray is normal. [2006, amended 2011, amended 2016]

If a prospective or current healthcare worker who is Mantoux-negative (see recommendations under "Diagnosing Latent TB in Adults") declines BCG vaccination, explain the risks and supplement the oral explanation with written advice. If the person still declines BCG vaccination, he or she should not work where there is a risk of exposure to TB. The employer will need to consider each case individually, taking account of employment and health and safety obligations. [2006, amended 2016]

Screen clinical students, agency and locum staff and contract ancillary workers who have contact with patients or clinical materials for TB to the same standard as new employees in healthcare environments, according to the recommendations set out above. Seek documentary evidence of screening to this standard from locum agencies and contractors who carry out their own screening. [2006]

NHS trusts arranging care for NHS patients in non-NHS settings should ensure that healthcare workers who have contact with patients or clinical materials in these settings have been screened for TB to the same standard as new employees in NHS settings. [2006]

Healthcare Environments: Occupational Health

Include reminders of the symptoms of TB, and the need for prompt reporting of such symptoms, with annual reminders about occupational health for staff who:

- Are in regular contact with TB patients or clinical materials or
- Have worked in a high-risk clinical setting for 4 weeks or longer.

Give one-off reminders after a TB incident on a ward. [2006]

If no documentary evidence of previous screening is available, screen staff in contact with patients or clinical material who are transferring jobs within the NHS as for new employees (see recommendations below under "Diagnosing Latent TB in Adults"). [2006]

Assess the risk of TB for a new healthcare worker who knows he or she is HIV-positive at the time of recruitment as part of the occupational health checks. [2006]

The employer, through the occupational health department, should be aware of the settings with increased risk of exposure to TB, and that these pose increased risks to HIV-positive healthcare workers. [2006]

Healthcare workers who are found to be HIV-positive during employment should have medical and occupational assessments of TB risk, and may need to modify their work to reduce exposure. [2006]

Latent TB

Diagnosing Latent TB in Adults

Offer Mantoux[1] testing to diagnose latent TB in adults aged 18 to 65 who are close contacts of a person with pulmonary or laryngeal TB.

- If the Mantoux test is inconclusive, refer the person to a TB specialist.
- If the Mantoux test is positive (an induration of 5 mm or larger, regardless of BCG history), assess for active TB (see "Active TB" below).
- If the Mantoux test is positive but a diagnosis of active TB is excluded, consider an interferon gamma release assay if more evidence of infection is needed to decide on treatment. This could be, for example, if the person needs enhanced case management or if there could be adverse events from treatment.
- If the Mantoux is positive, and if an IGRA was done and that is also positive, offer them treatment for latent TB infections (see "Managing Latent TB in All Age Groups" below) [2011, amended 2016]

Adults Who Are Immunocompromised

In adults who are anticipated to be or are currently immunocompromised, do a risk assessment to establish whether testing should be offered, taking into account their:

- Risk of progression to active TB based on how severely they are immunocompromised and for how long they have been immunocompromised
- Risk factors for TB infection, such as country of birth or recent contact with an index case with suspected infectious or confirmed pulmonary or laryngeal TB [new 2016]

For adults who are severely immunocompromised, such as those with HIV and CD4 counts of fewer than 200 cells/mm^3, or after solid organ or allogeneic stem cell transplant, offer an interferon-gamma release assay and a concurrent Mantoux test.

- If either test is positive (for Mantoux, this is an induration of 5 mm or larger, regardless of BCG history), assess for active TB.
- If this assessment is negative, offer them treatment for latent TB infection. [new 2016]

For other adults who are immunocompromised, consider an interferon-gamma release assay alone or an interferon-gamma release assay with a concurrent Mantoux test.

- If either test is positive (for Mantoux, this is an induration of 5 mm or larger, regardless of BCG history), assess for active TB.
- If this assessment is negative, offer them treatment for latent TB infection. [new 2016]

Healthcare Workers

Offer a Mantoux test to new NHS employees who will be in contact with patients or clinical materials, if the employees:

- Are not new entrants from high-incidence countries and
- Have not had BCG vaccination (for example, they are without a BCG scar, other documentation or a reliable history)

If the Mantoux test is positive, offer an interferon-gamma release assay. If this is positive, assess for active TB; if this assessment is negative, offer them treatment for latent TB infection. [2011, amended 2016]

Offer a Mantoux test to new NHS employees who are from a high-incidence country.

- If the Mantoux test is positive (5 mm or larger, regardless of BCG history), assess for active TB; if this assessment is negative, offer them treatment for latent TB infection.
- If Mantoux testing is unavailable, offer an interferon-gamma release assay. [new 2016]

Offer an interferon-gamma release assay to new NHS employees who have had contact with patients in settings where TB is highly prevalent:

- If the interferon-gamma release assay is positive, assess for active TB and
- If this assessment is negative, offer them treatment for latent TB infection [2011, amended 2016]

Healthcare workers who are immunocompromised should be screened in the same way as other people who are immunocompromised (see

recommendations above). [2011]

Diagnosing Latent TB in Children and Young People

Only consider using interferon-gamma release assays alone in children and young people if Mantoux testing is not available or is impractical. This includes for example, situations in which large numbers need to be tested (see the section "Incident and Outbreak Response" below and the recommendation under "Diagnosing Latent TB in All Age Groups" below). [new 2016]

Refer children younger than 2 years and in close contact with people with smear-negative pulmonary or laryngeal TB to a specialist to determine what testing strategy for latent TB should be done. This should be a paediatrician with experience and training in TB, or a general paediatrician with advice from a specialised clinician. [new 2016]

If a neonate has been in close contact with people with smear-positive pulmonary or laryngeal TB who have not had at least 2 weeks of anti-TB treatment:

- Assess for active TB (see under "Active TB" below).
- Start isoniazid (with pyridoxine).
- Carry out a Mantoux test after 6 weeks of treatment.
- If the Mantoux test is inconclusive, refer the child to a TB specialist.
- If the Mantoux test is positive (5 mm or larger, regardless of BCG history), reassess for active TB; if this assessment is negative, continue isoniazid (with pyridoxine) for a total of 6 months.
- If the Mantoux test is negative, reassess for active TB and consider an interferon-gamma release assay:
    - If the interferon-gamma release assay is negative then stop isoniazid (and pyridoxine) and give a BCG vaccination (see "BCG Vaccination" above)
    - If the interferon-gamma release assay is positive, reassess for active TB; if this assessment for active TB is negative, continue isoniazid (with pyridoxine) for a total of 6 months. [new 2016]

If a child aged between 4 weeks and 2 years has been in close contact with people with smear-positive pulmonary or laryngeal TB who have not had at least 2 weeks of anti-TB treatment:

- Assess for active TB.
- Start treatment for latent TB (see "Managing Latent TB in All Age Groups" and "Managing Latent TB in Children and Young People" below) and carry out a Mantoux test.
- If the Mantoux test is inconclusive, refer the child to a TB specialist.
- If the Mantoux test is positive (5 mm or larger, regardless of BCG history), reassess for active TB; if this assessment is negative, complete treatment for latent TB.
- If the Mantoux test is negative, continue treatment for latent TB, reassess for active TB after 6 weeks and repeat the Mantoux test:
    - If the Mantoux test is negative, consider an interferon-gamma release assay.
    - If the interferon-gamma release assay is negative, treatment for latent TB may be stopped; give a BCG vaccination if the child has not already had one.
    - If either test is positive, reassess for active TB; if this assessment is negative, complete treatment for latent TB. [new 2016]

If a child or young person aged between 2 and 17 years has been in close contact with people with pulmonary or laryngeal TB:

- Offer Mantoux testing.
- If the Mantoux test is inconclusive, refer the child or young person to a TB specialist.
- If the Mantoux test is positive (5 mm or larger, regardless of BCG history), assess for active TB; if this assessment is negative, offer them treatment for latent TB infection.
- If the initial Mantoux test is negative, offer an interferon-gamma release assay after 6 weeks and repeat the Mantoux test. [new 2016]

Immunocompromised Children and Young People

If latent TB is suspected in children and young people who are anticipated to be or are currently immunocompromised (for example, if they are from a high incidence country or have been in close contact with people with suspected infectious or confirmed pulmonary or laryngeal TB), refer to a TB specialist. [2016]

Diagnosing Latent TB in All Age Groups

New Entrants from High-Incidence Countries

Offer Mantoux testing as the initial diagnostic test for latent TB infection in people who have recently arrived from a high-incidence country who present to healthcare services. If the Mantoux test is positive (5 mm or larger, regardless of BCG history):

- Assess for active TB (see recommendations under "Active TB" below) and
- If this assessment is negative, offer them treatment for latent TB infection (see recommendations under "Managing Latent TB in All Age Groups," "Managing Latent TB in Adults, and "Managing Latent TB in Children and Young People" below).

If Mantoux testing is unavailable, offer an interferon-gamma release assay. [new 2016]

Contacts – Incident Situation

In an incident situation when large numbers of people may need to be screened, consider a single interferon-gamma release assay for people aged 18 to 65 years. For children and young people, follow recommendations under "Diagnosing Latent TB in Children and Young People" above. [2011, amended 2016]

Under-served Groups

Offer people younger than 65 years from under-served groups a single interferon-gamma release assay. [2011, amended 2016]

Substance misuse services with access to an interferon-gamma release assay should provide testing for people younger than 65 years who misuse substances if they:

- Live in a high incidence area
- Are likely to be involved with substance misuse services or other support services on a regular basis (for example, for opioid substitution therapy), when support should be available for directly observed preventive therapy [2012, amended 2016]

In high incidence areas (and at prisons that receive prisoners from high incidence areas), prison health services should offer an interferon-gamma release assay for TB to inmates younger than 65 years who are in regular contact with substance misuse services or other support services. This is provided arrangements have been made for this support to continue after release. [2012, amended 2016]

Substance misuse services and prison health services should incorporate interferon-gamma release assay testing with screening for hepatitis B and C, and HIV testing. They should refer prisoners and people who misuse substances with positive interferon-gamma release assays to local multidisciplinary TB teams for further clinical investigations. For prisoners, these investigations should be done in the prison if practically possible. [2012, amended 2016]

If the interferon-gamma release assay is positive, assess for active TB (see sections under "Active TB" below); if this assessment is negative, offer them treatment for latent TB infection (see recommendations under "Managing Latent TB in All Age Groups," "Managing Latent TB in Adults, and "Managing Latent TB in Children and Young People" below). [new 2016]

Managing Latent TB in All Age Groups

Be aware that certain groups of people with latent TB are at increased risk of going on to develop active TB, including people who:

- Are HIV-positive
- Are younger than 5 years
- Have excessive alcohol intake
- Are injecting drug users
- Have had solid organ transplantation
- Have a haematological malignancy
- Are having chemotherapy
- Have had a jejunoileal bypass
- Have diabetes
- Have chronic kidney disease or receive haemodialysis
- Have had a gastrectomy
- Are having treatment with anti-tumour necrosis factor-alpha or other biologic agents
- Have silicosis [new 2016]

For people, including those with HIV, aged younger than 65 years with evidence of latent TB who have been in close contact with people who have suspected infectious or confirmed active pulmonary or laryngeal drug-sensitive TB, offer either of the following drug treatments:

- 3 months of isoniazid (with pyridoxine) and rifampicin or
- 6 months of isoniazid (with pyridoxine) [new 2016]

Base the choice of regimen on the person's clinical circumstances. Offer:

- 3 months of isoniazid (with pyridoxine) and rifampicin to people younger than 35 years if hepatotoxicity is a concern after an assessment of both liver function (including transaminase levels) and risk factors
- 6 months of isoniazid (with pyridoxine) if interactions with rifamycins are a concern, for example, in people with HIV or who have had a transplant [new 2016]

Clearly explain the risks and potential benefits of each treatment regimen. In discussion with the person, select a suitable regimen if they wish to proceed with preventive treatment. [new 2016]

If a person also has severe liver disease, for example, Child-Pugh level B or C, work with a specialist multidisciplinary team with experience of managing TB and liver disease. [new 2016]

Manage treatment with caution, ensuring careful monitoring of liver function, in:

- People with non-severe liver disease
- People with abnormal liver function (including abnormal transaminase levels) before starting treatment for latent TB infection
- People who misuse alcohol or drugs [new 2016]

Ensure people having treatment for latent TB who also have social risk factors, such as misusing alcohol or drugs or being homeless, are linked to support services. They should also have an assessment of social needs and stability, including potential barriers to adherence or treatment completion (see recommendations under "Adherence, Treatment Completion and Follow-up" below). [new 2016]

People in the groups listed in the first recommendation in this section who do not have treatment for latent TB, as specified in the recommendations above, for any reason should be advised of the risks and symptoms of TB (on the basis of an individual risk assessment), usually in a standard letter of the type referred to as 'Inform and advise' information (see recommendations under "Providing information for the Public about TB" above). [new 2016]

Managing Latent TB in Adults

For adults between the ages of 35 and 65 years, offer drug treatments only if hepatotoxicity is not a concern. [new 2016]

Offer testing for HIV before starting treatment for latent TB. See NICE guidelines on increasing the uptake of HIV testing among black Africans in England and increasing the uptake of HIV testing among men who have sex with men. [new 2016]

Offer adults testing for hepatitis B and C before starting treatment for latent TB. See the NICE guideline on hepatitis B and C: ways to promote and offer testing to people at increased risk of infection and the NGC summary of the NICE guideline Hepatitis B (chronic). Diagnosis and management of chronic hepatitis B in children, young people and adults. [new 2016]

Managing Latent TB in Children and Young People

Consider testing children and young people for hepatitis B and C before starting treatment for latent TB. See NICE guideline on hepatitis B and C: ways to promote and offer testing to people at increased risk of infection and the NGC summary of the NICE guideline Hepatitis B (chronic). Diagnosis and management of chronic hepatitis B in children, young people and adults. [new 2016]

Active TB

Diagnosing Active TB in All Age Groups

If TB is a possibility, microbiology staff should consider carrying out TB culture on samples (see recommendations under "Diagnosing Pulmonary [Including Laryngeal] TB in All Age Groups" below), even if it is not requested. [2006, amended 2016]

If there are clinical signs and symptoms consistent with a diagnosis of TB, start treatment without waiting for culture results. [2006]

Consider completing the standard recommended regimen (see recommendations under "Managing Active TB in All Age Groups" below), even if subsequent culture results are negative. [2006, amended 2016]

Diagnosing Pulmonary (Including Laryngeal) TB in All Age Groups

Take a chest X-ray; do further diagnostic investigations (as detailed in Table 1 in the original guideline document) if chest X-ray appearances suggest TB. [2016]

Send multiple respiratory samples (3 deep cough sputum samples, preferably including 1 early morning sample) for TB microscopy and culture. [2016]

- This should be before starting treatment if possible or, failing that, within 7 days of starting treatment in people with life-threatening disease. [2006, amended 2016]
- Obtain spontaneously-produced, deep cough sputum samples if possible, otherwise use:
  - 3 gastric lavages or 3 inductions of sputum in children and young people (see "Infection Control: Healthcare Settings" below) [new 2016] or
  - Induction of sputum or bronchoscopy and lavage in adults [2006, amended 2016]
- Laboratory practices should be in accordance with the UK's Standards for Microbiology Investigations. [new 2016]

Send samples for TB culture from autopsy samples if pulmonary or laryngeal TB is a possibility. [2006, amended 2016]

Diagnosing Pulmonary (Including Laryngeal) TB in Adults

Request rapid diagnostic nucleic acid amplification tests for the *M. tuberculosis* complex (*M. tuberculosis*, *M. bovis*, *M. africanum*) on primary specimens (listed in Table 1 in the original guideline document) if there is clinical suspicion of TB disease, and:

- The person has HIV or
- Rapid information about mycobacterial species would alter the person's care or
- The need for a large contact-tracing initiative is being explored [new 2016]

Diagnosing Pulmonary (Including Laryngeal) TB in Children and Young People

In children aged 15 years or younger with suspected pulmonary TB, offer rapid diagnostic nucleic acid amplification tests for the *M. tuberculosis* complex (*M. tuberculosis*, *M. bovis*, *M. africanum*). Usually only 1 nucleic acid amplification test is needed per specimen type (for example, spontaneous sputum, induced sputum or gastric lavage; see Table 1 in the original guideline document). [new 2016]

In young people aged 16 to 18 years use the same criteria as in adults to decide whether to request rapid diagnostic nucleic acid amplification tests (see Table 1 in the original guideline document). [new 2016]

Either a paediatrician with experience and training in TB or a general paediatrician with advice from a specialised clinician should investigate and manage TB in children and young people. [new 2016]

An expert in paediatric TB may request interferon-gamma release assays and tuberculin skin tests. Interpret these together with other diagnostic tools (such as history taking, clinical examination and imaging). [new 2016]

Diagnosing Extrapulmonary TB in All Age Groups

Discuss the advantages and disadvantages of both biopsy and needle aspiration with the patient, with the aim of obtaining adequate material for diagnosis. [2006]

Do not place part or all of any of the samples in formalin (or other fixative agent) when sending for TB culture. [2006, amended 2016]

Think about a diagnosis of extrapulmonary TB even if rapid diagnostic tests in, for example, cerebrospinal fluid, pleural fluid or ascitic fluid are negative. [new 2016]

Offer all patients presenting with extrapulmonary TB a chest X-ray and, if possible, culture of a spontaneously-produced respiratory sample to exclude or confirm coexisting pulmonary TB (see sections above). Also, consider site-specific tests as described below to exclude or confirm additional sites of TB. [new 2016]

Refer to an expert for sites not listed in the guideline, including TB of the eye and other rare sites of disease. [new 2016]

Pleural TB

Use the site-specific investigations listed in Table 2 in the original guideline document to diagnose and assess pleural TB. [new 2016]

Central Nervous System TB

Use the site-specific investigations listed in Table 3 in the original guideline document to diagnose and assess central nervous system TB. [new 2016]

Offer a tomography (CT) or magnetic resonance image (MRI) scan to people in whom central nervous system involvement is suspected. [2016]

Offer treatment for TB meningitis if clinical signs and other laboratory findings are consistent with the diagnosis, even if a rapid diagnostic test is negative. [new 2016]

Lymph Node TB (Including Intrathoracic Mediastinal Adenopathy)

Use the site-specific investigations listed in Table 4 in the original guideline document to diagnose and assess lymph node TB (including intrathoracic mediastinal adenopathy). [new 2016]

Pericardial TB

Use the site-specific investigations listed in Table 5 in the original guideline document to diagnose and assess pericardial TB. [new 2016]

Gastrointestinal TB

Use the site-specific investigations listed in Table 6 in the original guideline document to diagnose and assess gastrointestinal TB. [new 2016]

Genitourinary TB

Use the site-specific investigations listed in Table 7 in the original guideline document to diagnose and assess genitourinary TB. [new 2016]

Bone and Joint TB

Use the site-specific investigations listed in Table 8 in the original guideline document to diagnose and assess bone and joint TB. [new 2016]

Disseminated TB

Use the site-specific investigations listed in Table 9 in the original guideline document to diagnose and assess disseminated TB. [new 2016]

Skin TB

Use the site-specific investigations listed in Table 10 in the original guideline document to diagnose and assess skin TB. [2016]

Localised Tuberculous Abscess

Use the site-specific investigations listed in Table 11 in the original guideline document to diagnose and assess TB in a localised, tuberculous abscess at a site other than a lymph node. [2016]

Rapid-Access Radiology and Other Investigation Results – Referral to Multidisciplinary TB Team Process

Local hospitals, clinical commissioning groups and the local multidisciplinary team should consider developing a local pathway for people with imaging highly suggestive of active TB. The pathway should enable them to be referred by the radiology department by the next working day to multidisciplinary TB teams. Consider including the following in the pathway:

- Agreed standardised radiology codes to identify imaging investigations highly suggestive of active TB
- Regular liaison between multidisciplinary TB teams and the radiology department (for example, weekly) to ensure all patients have been referred to the multidisciplinary team for triage using the agreed local mechanism or pathway [new 2016]

Report results of all pathology or other diagnostic results suggesting TB to the multidisciplinary TB team and clinicians who ask for them. [new 2016]

Direct Referral from Emergency Departments to Multidisciplinary TB Team

Commissioners and multidisciplinary teams should consider working with emergency departments to develop direct referral pathways for people with suspected active TB so that:

- The local multidisciplinary team is informed of all suspected cases of TB using the appropriate process
- Referral is accepted from any appropriate healthcare professional, for example an on-call radiologist [new 2016]

Emergency department clinicians should ensure first-line diagnostic tests for TB are performed on anyone presenting with suspected TB (see Table 1 in the original guideline document). [new 2016]

Emergency departments should consider carrying out audits of their direct referrals because of suspected active TB and the outcomes of diagnosis. [new 2016]

Multidisciplinary TB teams should consider training emergency department staff in:

- Using approaches that do not stigmatise people with TB
- Giving people with TB appropriate advice (see recommendations under "Raising and Sustaining Awareness of TB" and "Providing Information for the Public about TB" above and under "Infection Control" below) [new 2016]

Managing Active TB in All Age Groups

Standard Treatment

Once a diagnosis of active TB is made:

- The clinician responsible for care should refer the person with TB to a clinician with training in, and experience of, the specialised care of people with TB.
- The TB service should include specialised nurses and health visitors.
- Active TB in children should be managed by a TB specialist (see recommendation under "Diagnosing Pulmonary (Including Laryngeal) TB in Children and Young People" above), and by paediatric trained nursing staff, where possible.

If these arrangements are not possible, seek advice from more specialised colleagues throughout the treatment period. [2016]

For people with active TB without central nervous system involvement, offer:

- Isoniazid (with pyridoxine), rifampicin, pyrazinamide and ethambutol for 2 months then
- Isoniazid (with pyridoxine) and rifampicin for a further 4 months

Modify the treatment regimen according to drug susceptibility testing. [2016]

For people with active TB of the central nervous system, offer:

- Isoniazid (with pyridoxine), rifampicin, pyrazinamide and ethambutol for 2 months then
- Isoniazid (with pyridoxine) and rifampicin for a further 10 months

Modify the treatment regimen according to drug susceptibility testing. [2016]

Test people with active spinal TB who have neurological signs or symptoms for central nervous system involvement (see recommendation under "Central Nervous System TB" above). Manage direct spinal cord involvement (for example, a spinal cord tuberculoma) as TB of the central nervous system. [2016]

For people with active spinal TB without central nervous system involvement, do not extend treatment beyond 6 months for residual effects (for example, persistent bending of the spine or vertebral loss). [2016]

Test people with disseminated (including miliary) TB who have neurological signs or symptoms for central nervous system involvement. If there is evidence of central nervous system involvement, treat as for TB of the central nervous system. [2016]

Treat active peripheral lymph node TB in people who have had an affected gland surgically removed with the standard recommended regimen. [new 2016]

For people with active TB of the lymph nodes, do not routinely extend treatment beyond 6 months for newly enlarged lymph nodes or sinus formation, or for residual enlargement of the lymph nodes or sinuses. [new 2016]

Dosing of Regimens

Use fixed-dose combination tablets as part of any TB treatment regimen. [2006]

Do not offer anti-TB treatment dosing regimens of fewer than 3 times per week. [2006, amended 2016]

Offer a daily dosing schedule to people with active pulmonary TB. [2006, amended 2016]

Consider a daily dosing schedule as first choice in people with active extrapulmonary TB. [2006, amended 2016]

Consider 3 times weekly dosing for people with active TB only if:

- A risk assessment identifies a need for directly observed therapy and enhanced case management (see "Adherence, Treatment Completion and Follow-up" below) and
- Daily directly observed therapy is not possible [2006, amended 2016]

People with Comorbidities or Coexisting Conditions

If the person has a comorbidity or coexisting condition such as:

- HIV or
- Severe liver disease, for example, Child-Pugh level B or C or
- Stage 4 or 5 chronic kidney disease (a glomerular filtration rate of <30 ml/minute/ 1.73 m^2) or
- Diabetes or
- Eye disease or impaired vision or
- Pregnancy or breastfeeding or
- A history of alcohol or substance misuse

Work with a specialist multidisciplinary team with experience of managing TB and the comorbidity or coexisting condition. [new 2016]

For people with HIV and active TB without central nervous system involvement, do not routinely extend treatment beyond 6months. [new 2016]

For people with HIV and active TB with central nervous system involvement, do not routinely extend treatment beyond 12 months. [new 2016]

Take into account drug-to-drug interactions when co-prescribing antiretroviral and anti-TB drugs. [new 2016]

Adjunctive Corticosteroids

Central Nervous System TB

At the start of an anti-TB treatment regimen, offer people with active TB of the central nervous system dexamethasone or prednisolone, initially at a high dose with gradual withdrawal over 4 to 8 weeks. An example of a suitable regimen is listed in Table 12 in the original guideline document. [new 2016]

At the start of an anti-TB treatment regimen, offer children and young people with active TB of the central nervous system dexamethasone or prednisolone. This should initially be at a high dose with gradual withdrawal over 4 to 8 weeks in line with the British National Formulary for Children. [new 2016]

Pericardial TB

At the start of an anti-TB treatment regimen, offer adults with active pericardial TB oral prednisolone at a starting dose of 60 mg/day, gradually withdrawing it 2 to 3 weeks after starting treatment. [2016]

At the start of an anti-TB treatment regimen, offer children and young people with active pericardial TB oral prednisolone in line with the British National Formulary for Children. Gradually withdraw prednisolone 2 to 3 weeks after starting treatment. [2016]

Adjunctive Surgery

If surgery is indicated, the surgeon should fully explain what is involved to the person, either with or after consulting a TB specialist. Discuss the possible benefits and risks with the person and their family members or carers, as appropriate, so that they can make an informed decision. [new 2016]

Central Nervous System TB

Consider referring people with TB of the central nervous system for surgery as a therapeutic intervention only if there is evidence of raised intracranial pressure. [new 2016]

Spinal TB

Do not routinely refer people with spinal TB for surgery to eradicate the disease. [new 2016]

Consider referring people with spinal TB for surgery if there is spinal instability or evidence of spinal cord compression. [new 2016]

Drug Resistant TB

Multidrug-Resistant TB

For people with clinically suspected TB, a TB specialist should request rapid diagnostic nucleic acid amplification tests for rifampicin resistance on primary specimens if a risk assessment for multidrug resistance identifies any of the following risk factors:

- History of previous TB drug treatment, particularly if there was known to be poor adherence to that treatment
- Contact with a known case of multidrug-resistant TB
- Birth or residence in a country in which the World Health Organization reports that a high proportion (5% or more) of new TB cases are multidrug-resistant

Start infection control measures (see recommendations under "Infection Control" below). [new 2016]

If the rapid diagnostic nucleic acid amplification test for rifampicin resistance is positive:

- Continue infection control measures until pulmonary or laryngeal disease has been excluded.
- Manage treatment along with a multidisciplinary team with experience of managing multidrug-resistant TB (see recommendations under "Service Organisation" below).
- Offer a treatment regimen involving at least 6 drugs to which the mycobacterium is likely to be sensitive.
- Test for resistance to second-line drugs. [new 2016]

If the rapid diagnostic nucleic acid amplification test for the *M. tuberculosis* complex is positive but rifampicin resistance is not detected, treat as drug-susceptible TB with the standard regimen (see "Managing Active TB in All Age Groups" above). [new 2016]

If the rapid diagnostic nucleic acid amplification test for the *M. tuberculosis* complex is negative in a person at high risk of multidrug-resistant TB:

- Obtain further specimens for nucleic acid amplification testing and culture, if possible.
- Use rapid rifampicin resistance detection on cultures that become positive for the *M. tuberculosis* complex.
- Consider waiting for the results of further tests before starting treatment if the person is well.
- If urgent treatment is needed, consider managing as multidrug-resistant TB until sensitivity results are available. [new 2016]

When definitive phenotypic susceptibility results are available, modify treatment as needed (see "Managing Active TB in All Age Groups" above and" Drug-Resistant TB (Excluding Multidrug- and Extensively Drug-Resistant TB)" below). [new 2016]

Consider more intensive clinical follow-up for people with multidrug-resistant TB. This includes people having directly observed therapy (see "Adherence, Treatment Completion and Follow-up" below) throughout treatment because of the complexity of treatment and risk of adverse events. [new 2016]

Discuss the options for organising care for people with multidrug-resistant TB with clinicians who specialise in this. Seek the person's views and take them into account, and consider shared care (see "Service Organisation" below). [2006]

Consider surgery as a therapeutic intervention in people with potentially resectable multidrug-resistant disease if:

- Optimal medical therapy under direct observation has not worked or
- Medical therapy is likely to fail because of extensively drug-resistant TB [new 2016]

Drug-Resistant TB (Excluding Multidrug- and Extensively Drug-Resistant TB)

For people with TB, without central nervous system involvement, that is resistant to just 1 drug consider the treatments in Table 13 in the original guideline document. [new 2016]

For people with drug-resistant TB and central nervous system involvement, involve a TB specialist with experience in managing drug-resistant TB in decisions about the most appropriate regimen and the duration of treatment. [new 2016]

Infection Control

Note: NICE has also produced general guidelines on the prevention and control of healthcare-associated infections in primary and community care, and the prevention and control of healthcare-associated infections . (See the NGC summary of the NICE guideline Infection. Prevention and control of healthcare-associated infections in primary and community care.)

Healthcare Settings

Ensure healthcare settings can promptly identify people with suspected infectious or confirmed pulmonary or laryngeal TB before or at presentation. Ensure people working in the settings follow the recommendations about testing and treatments (see "Latent TB," "Active TB," and "Drug-Resistant TB" sections above). [new 2016]

Put people with suspected infectious or confirmed pulmonary or laryngeal TB who will remain in a hospital setting (including emergency, outpatients or inpatient care) in a single room. If this is not possible, keep the person's waiting times to a minimum. This may involve prioritising their care above that of other patients. [new 2016]

Minimise the number and duration of visits a person with TB makes to an outpatient department while they are still infectious. To minimise the risk of infection, people with infectious TB should be seen at times or in places away from other people. [new 2016]

In hospital settings, risk assess people with suspected infectious or confirmed pulmonary TB for multidrug-resistant TB (see recommendation under "Drug-Resistant TB" above). Care for people deemed to be at low risk in a single room, as a minimum. For people deemed to be at high risk:

- Provide care in a negative pressure room and
- Have specimens sent for rapid diagnostic tests, such as nucleic acid amplification tests [new 2016]

Unless there is a clear clinical or public health need, such as homelessness, people with suspected infectious or confirmed pulmonary TB should not be admitted to hospital for diagnostic tests or for care. [2006, amended 2016]

Do not admit people with suspected infectious or confirmed pulmonary TB to a ward containing people who are immunocompromised, such as transplant recipients, people with HIV and those on anti-tumour necrosis factor alpha or other biologics, unless they can be cared for in a negative pressure room on the same ward. [new 2016]

Assess any visitors to a child with suspected active TB in hospital for symptoms of infectious TB, and keep them separate from other people until they have been excluded as a source of infection (see recommendations under "Diagnosing Latent TB in Adults," "Diagnosing Latent TB in Children and Young People," and "Diagnosing Latent TB in All Age Groups" above and "Contact Tracing" below). [new 2016]

Care for people with a continuing clinical or public health need for admission with pulmonary TB in a single room (as a minimum) until they have completed 2 weeks of the standard treatment regimen (see "Managing Active TB in All Age Groups" above) if they:

- Are unlikely to be rifampicin resistant (that is, do not have risk factors for multidrug-resistant TB) or
- Have negative rifampicin resistance on nucleic acid amplification test or culture [new 2016]

Consider de-escalating isolation after 2 weeks of treatment, taking into account the risks and benefits, if:

- The person is showing tolerance to the prescribed treatment
- There is agreement to adhere to treatment
- There is resolution of cough
- There is definite clinical improvement on treatment; for example, remaining afebrile for a week
- There are not immunocompromised people, such as transplant recipients, people with HIV and those on anti-tumour necrosis factor alpha or other biologics, in the same accommodation
- The person's initial smear grade was not high; for example, 2 or less
- There is not extensive pulmonary involvement, including cavitation
- There is no laryngeal TB [new 2016]

In people who may have TB, only carry out aerosol-generating procedures such as bronchoscopy, sputum induction or nebuliser treatment in an appropriately engineered and ventilated area (ideally a negative pressure room). [new 2016]

Consider discharging from hospital people:

- Who do not have a continuing clinical or public health need for admission with pulmonary TB and
- Who are unlikely to be rifampicin resistant (that is, do not have risk factors for multidrug-resistant TB) or
- Who have negative rifampicin resistance on nucleic acid amplification test or culture

If discharged, the person should avoid congregate settings for the first 2 weeks of their treatment. [new 2016]

Explain to inpatients with suspected infectious or confirmed pulmonary or laryngeal TB that they will need to wear a surgical mask in the hospital whenever they leave their room. Ask them to continue wearing it until they have had at least 2 weeks of treatment. [2016]

Offer people advice on simple respiratory hygiene measures. [new 2016]

care Settings

In non-healthcare settings catering for large numbers of people and populations at high risk of TB (such as detention settings, residential hostels and day centres):

- Promote simple respiratory hygiene
- Ensure awareness of symptoms of potentially infectious TB to enable prompt healthcare referral
- Work with the local public health team and the local authority to ensure accommodation for people with TB
- Ensure adequate ventilation [new 2016]

In prisons or immigration removal centres, everyone with X-ray changes indicative of active TB, as well as those with symptoms who are awaiting X-ray, should be isolated in an adequately ventilated individual room or cell. Prisoners and detainees should be retained on medical hold until they have:

- Proven smear-negative and had an X-ray that does not suggest active TB or
- Had a negative risk assessment for multidrug-resistant TB and completed 2 weeks of the standard treatment regimen [2012, amended 2016]

Multidrug-Resistant TB

If people with suspected or known infectious multidrug-resistant TB are admitted to hospital, admit them to a negative pressure room. If none is available locally, transfer them to a hospital that has these facilities and a clinician experienced in managing complex drug-resistant cases. Carry out care in a negative pressure room for people with:

- Suspected multidrug-resistant TB, until non-resistance is confirmed
- Confirmed multidrug-resistant TB, until they have 3 negative smears at weekly intervals and ideally have a negative culture [new 2016]

As soon as possible, explore options to reduce the psychosocial impact of prolonged isolation. For example, through providing free access to internet, telephone and television, and accompanied walks in the open air. [new 2016]

Consider earlier discharge for people with confirmed multidrug-resistant TB, if there are suitable facilities for home isolation and the person will adhere to the care plan. [new 2016]

For people with confirmed multidrug-resistant TB whose symptoms have improved and who are unable to produce sputum, discharge decisions should be taken by the multidisciplinary team and the health protection team. [new 2016]

Staff and visitors should wear filtering face piece (FFP3) masks during contact with a person with suspected or known multidrug-resistant TB while the person is thought to be infectious. [2016]

Before deciding to discharge a person with suspected or known multidrug-resistant TB from hospital, agree with the person and their carers secure arrangements for supervising and administering all anti-TB therapy. [2016]

Discuss the decision to discharge a person with suspected or known multidrug-resistant TB with:

- The infection control team and
- The local microbiologist and
- The local TB service and
- The health protection team [2016]

Ensure negative pressure rooms used for infection control in multidrug-resistant TB meet the standards of the Interdepartmental Working Group on Tuberculosis, and are clearly identified for staff, for example by a standard sign. Keep such signs up to date. [2016]

Case Finding

Contact Tracing

Human to Human Transmission

Once a person has been diagnosed with active TB, the diagnosing physician should inform relevant colleagues so that the need for contact tracing can be assessed without delay. Contact tracing should not be delayed until notification. [2006]

Offer screening to the close contacts of any person with pulmonary or laryngeal TB. [2006, amended 2016]

Assess symptomatic close contacts for active TB (see relevant diagnostic sections under "Active TB" above). [new 2016]

In asymptomatic close contacts younger than 65 years, consider standard testing for latent TB (see relevant diagnostic sections under "Latent TB" above), followed by consideration of BCG vaccination (see "BCG Vaccination" above) or treatment for latent TB infection (see relevant management sections under "Latent TB" above) once active TB has been ruled out for people who:

- Are previously unvaccinated and
- Are contacts of a person with smear-positive pulmonary or laryngeal TB and
- Are Mantoux[1]-negative [2006, amended 2016]

In asymptomatic close contacts older than 65 years, consider a chest X-ray (if there are no contraindications), possibly leading to further investigation for active TB. [2006, amended 2016]

Do not routinely assess social contacts of people with TB, who will include most workplace contacts. [2006, amended 2016]

Assess the need for tracing social contacts of people with pulmonary or laryngeal TB if:

- The index case is judged to be particularly infectious (for example, evidenced by transmission to close contacts) or
- Any social contacts are known to possess features that put them at high risk of going on to develop active TB [2006, amended 2016]

Offer 'inform and advise' information to all contacts of people with smear-positive TB (see recommendations under "Providing Information for the Public about TB" above). [2006]

Cases on an Aircraft

After diagnosis of TB in an aircraft traveller, do not routinely carry out contact tracing of fellow passengers. [2006, amended 2016]

The notifying clinician should inform the relevant consultant in communicable disease control or health protection if:

- Less than 3 months has elapsed since the flight and the flight was longer than 8 hours and
- The index case is smear-positive and either
    - The index case has multidrug-resistant TB or
    - The index case coughed frequently during the flight [2006]

The consultant in communicable disease control or health protection should provide the airline with 'inform and advise' information to send to passengers seated in the same part of the aircraft as the index case. [2006, amended 2016]

If the TB index case is an aircraft crew member, contact tracing of passengers should not routinely take place. [2006]

If the TB index case is an aircraft crew member, contact tracing of other members of staff is appropriate, in accordance with the usual principles for screening workplace colleagues. [2006]

Cases in Schools

After diagnosis of TB in a school pupil or member of staff, the consultant in communicable disease control or health protection should be prepared to explain the prevention and control procedures to staff, parents and the press. Advice on managing these incidents and their public relations is available from the Public Health England health protection team and the local authority. [2006, amended 2016]

If a school pupil is diagnosed with smear-positive TB, carry out a risk assessment of the need to test the rest of his or her class (if there is a single class group), or the rest of the year group who share classes, as part of contact tracing. [2006]

If a teacher has smear-positive TB, assess the pupils in his or her classes during the preceding 3 months as part of contact tracing. [2006]

Consider extending contact tracing in schools to include children and teachers involved in extracurricular activities, and non-teaching staff, on the basis of:

- The degree of infectivity of the index case
- The length of time the index case was in contact with others
- Whether contacts are unusually susceptible to infection
- The proximity of contact [2006, amended 2016]

Treat secondary cases of smear-positive TB as index cases for contact tracing. [2006]

If the index case of a school pupil's TB infection is not found, and the child is not in a high-risk group for TB, contact tracing and screening (by either symptom enquiry or chest X-ray) should be considered for all relevant members of staff at the school. [2006]

Cases in Community Childcare

When an adult who works in childcare (including people who provide childcare informally) is diagnosed with smear-positive TB, follow recommendations above. [2006, amended 2016]

Cases in Hospital Inpatients

If TB is diagnosed in a hospital inpatient, do a risk assessment. This should take into account:

- The degree of infectivity of the index case
- The length of time before the infectious patient was isolated
- Whether other patients are unusually susceptible to infection
- The proximity of contact [2006, amended 2016]

Carry out contact tracing and testing only for patients for whom the risk is regarded as significant. [2006]

Regard patients as at risk of infection if they spent more than 8 hours in the same bay as an inpatient with smear-positive TB who had a cough. Document the risk in the contact's clinical notes, for the attention of the contact's consultant. Give the contact 'inform and advise' information, and inform their GP. [2006]

If patients were exposed to a patient with smear-positive TB for long enough to be equivalent to close contacts (as determined by the risk assessment), or an exposed patient is known to be particularly susceptible to infection, manage their TB risk in the same way as close contacts. [2006, amended 2016]

If an inpatient with smear-positive TB is found to have multidrug-resistant TB, or if exposed patients are HIV positive, trace contacts following the Interdepartmental Working Group on Tuberculosis guidelines. [2006]

In cases of doubt when planning contact tracing after diagnosing smear-positive TB in an inpatient, seek further advice from the local or national Public Health England or Wales unit or people experienced in the field. [2006, amended 2016]

Opportunistic Case Finding

New Entrants from High Incidence Countries

Assess and manage TB in new entrants from high incidence countries who present to healthcare services as follows:

- Assess risk of HIV, including HIV prevalence rates in the country of origin, and take this into account when deciding whether to give a BCG vaccination.
- Offer testing for latent TB (see relevant diagnostic recommendations under "Latent TB" above).
- Assess for active TB if the test for latent TB is positive (see relevant diagnostic recommendations under "Active TB" above).
- Offer treatment to people aged 65 years or younger in whom active TB has been excluded but who have a positive Mantoux test or a positive interferon-gamma release assay for latent TB infection (see relevant management recommendations under "Latent TB" above).
- Consider offering BCG for unvaccinated people who are Mantoux- or interferon-gamma release assay-negative (see "BCG Vaccination" above).
- Give 'inform and advise' information to people who do not have active TB and are not being offered BCG or treatment for latent TB infection (see "Providing Information for the Public about TB" above). [2006, amended 2011 and 2016]

Primary care services should support local, community-based and voluntary organisations that work with vulnerable migrants to ensure they:

- Register with a primary care provider
- Know how to use NHS services (emergency or primary care) [2012]

Healthcare professionals, including primary care staff, responsible for testing new entrants should test all vulnerable migrants who have not previously been checked. This is regardless of when they arrived in England. People born in countries with an incidence of more than 150 per 100,000 per year should be made a priority for latent TB testing when they arrive here. [2012, amended 2016]

People Using Homeless or Substance Misuse Services

In areas of identified need (see "Local Needs Assessment" below), including major urban centres with a high incidence of TB, commissioners should:

- Ensure there is a programme of active case-finding using mobile X-ray in places where homeless people and people who misuse substances congregate (this includes: homeless day centres, rolling shelters, hostels and temporary shelters established as part of cold weather initiatives and venues housing needle and syringe programmes)
- Base the frequency of screening at any 1 location on population turnover
- Where local demand does not warrant a mobile X-ray team, consider commissioning mobile X-ray capacity from another area [2006, amended 2012]

Multidisciplinary TB teams should consider using simple incentives, such as providing hot drinks and snacks, to encourage people to attend for testing. [2006, amended 2012, amended 2016]

Commissioners of TB prevention and control programmes should consider offering people who are homeless and people who misuse substances other health interventions when they are screened for TB at a mobile X-ray unit. (Examples may include blood-borne virus screening, dentistry and podiatry services.) [2012]

Multidisciplinary TB teams should work closely with mobile X-ray teams and frontline staff in hostels and day centres to promote TB screening and to ensure appropriate onward referrals and follow-up. [2012]

Multidisciplinary TB teams should consider using peer educators to promote the uptake of TB screening in hostels and day centres. [2012]

Multidisciplinary TB teams should provide routine data to TB control boards on: screening uptake, referrals and the number of active TB cases identified. [2012]

People in Prisons or Immigration Removal Centres

Healthcare professionals in prisons and immigration removal centres should ensure prisoners and detainees are screened for TB within 48 hours of arrival. [2012]

Prisons with Department of Health-funded static digital X-ray facilities for TB screening should X-ray all new prisoners and detainees (including those being transferred from other establishments) if they have not had a chest X-ray in the past 6 months. This should take place within 48 hours of arrival. [2012]

Prison and immigration removal centre health staff should report all suspected and confirmed TB cases to the local multidisciplinary TB team within 1 working day. [2012]

Multidisciplinary TB staff should visit every confirmed TB case in a prison or immigration removal centre in their locality within 5 working days. [2012]

If a case of active TB is identified, the local Public Health England unit, in conjunction with the multidisciplinary TB team, should plan a contact investigations exercise. They should also consider using mobile X-ray to check for further cases. [2012]

Active Case Finding in Under-served Groups

Multidisciplinary TB teams should follow NICE recommendations on contact tracing (see section above). They should coordinate contact investigations at places where the person with TB spends significant amounts of time. Examples could include pubs, crack houses, parks and community centres. The aim is to help identify people who have been living with them and people they frequently socialise with. [2012]

Multidisciplinary TB teams dealing with someone from an under-served group should work alongside health and social care professionals known to them to help trace relevant contacts. They should also work in partnership with voluntary, community and statutory organisations to conduct

outreach contact investigations. [2012]

Multidisciplinary TB teams should, if available and appropriate, encourage peer educators or TB programme support workers to help with contact investigations involving under-served people who have complex social networks. [2012]

Multidisciplinary TB teams in discussion with local Public Health England health protection teams should consider using digital mobile X-ray for active case-finding in settings identified by looking at social networks as places where under-served people at risk congregate. They should also provide the necessary support so that multidisciplinary TB teams can use strain-typing and social network analysis to ascertain where transmission is occurring in the community. (Examples of transmission sites may include pubs, crack houses, hostels and day centres.) They should focus on active case-finding in the settings identified. [2012, amended 2016]

Incident and Outbreak Response

Multidisciplinary TB teams should coordinate incident or outbreak contact investigations at places where the person with active TB spends significant amounts of time. Examples include workplaces, schools, colleges, universities, childcare settings. Identify people that the person with TB frequently spends substantial time with, as outlined in "Contact Tracing" above. [new 2016]

Multidisciplinary TB teams should refer any incident in a congregate setting to the local Public Health England health protection team for risk assessment within 5 working days of suspicion of a potential incident. [new 2016]

TB control boards working with local health protection teams should, through local arrangements, mobilise existing staff or have access to an incident team that will:

- Undertake an incident risk assessment and provide advice
- Support or undertake contact investigations
- Provide information and communication support to the multidisciplinary TB team, the local director of public health, the setting in which the incident has occurred and the people affected including:
    - Written advice, printed or by email
    - Question and answer sessions
    - Telephone advice
    - Media engagement
- Gather and collate data, and report on outcomes to measure the effectiveness of the investigation (for example, offering testing to all people identified at risk and monitoring uptake)
- Report back to TB control boards at appropriate times. This includes when outcomes of initial investigation of people classified as close contacts are available. It also includes when a decision is made to broaden the investigation to the next stage using the concentric circle method for risk assessment. [new 2016]

When incidents have been identified, multidisciplinary TB teams in discussion with local Public Health England health protection teams should consider providing support for strain-typing and other analysis to ascertain where transmission is occurring. (Examples of transmission sites may include workplaces, schools, colleges, universities, childcare settings.) [new 2016]

In all types of contact investigation scenarios (active case finding, incident or outbreak investigations) multidisciplinary TB teams should investigate all people who have been in contact with children who have pulmonary or extrapulmonary TB to identify the primary source of infection. If necessary, they should look beyond immediate close contacts to find the source. [2012, amended 2016]

Adherence, Treatment Completion and Follow-up

Improving Adherence: Case Management Including Directly Observed Therapy

Allocate a named TB case manager to everyone with active TB as soon as possible after diagnosis (and within 5 days). The clinical team should tell each person who their named TB case manager is and provide contact details. [2006, 2012 amended 2016]

The TB case managers should work with the person diagnosed with TB to develop a health and social care plan, and support them to complete therapy successfully. The TB case manager should:

- Offer a risk assessment to every person with TB, to identify their needs and whether they should have enhanced case management including directly observed therapy
- Educate the person about TB and the treatment
- Develop an individual care plan after discussion with the person

- Gain the person's consent to the plan and agree a review date (for example, when moving from initiation to maintenance, or at each contact to ensure the person's needs are being met)
- Coordinate discharge planning, especially for people on directly observed therapy
- Involve representatives from other allied professions and key workers from all organisations who work with the person, if appropriate
- Explore appropriate ways that peers and voluntary organisations can provide support [2006, 2012, amended 2016]

Offer directly observed therapy as part of enhanced case management in people who:

- Do not adhere to treatment (or have not in the past) have been treated previously for TB
- Have a history of homelessness, drug or alcohol misuse
- Are currently in prison, or have been in the past 5 years
- Have a major psychiatric, memory or cognitive disorder
- Are in denial of the TB diagnosis
- Have multidrug-resistant TB
- Request directly observed therapy after discussion with the clinical team
- Are too ill to administer the treatment themselves [2012, amended 2016]

In children whose parents are members of any of the above groups, offer directly observed therapy as part of enhanced case management and include advice and support for parents to assist with treatment completion. [2016]

Re-evaluate the need for directly observed therapy throughout the course of TB treatment whenever the person's (or in the case of children, parents') circumstances change. [new 2016]

TB case managers should ensure the health and social care plan (particularly if directly observed therapy is needed) identifies why a person may not attend for diagnostic testing or follow a treatment plan, and how they can be encouraged to do so. It should also include ways to address issues such as fear of stigmatisation, support needs and/or cultural beliefs, and may include information on:

- Demographics (for example, age, nationality, place of birth, length of time in UK)
- All current prescribing regimens
- Housing needs and living situation, including looked-after children
- Substance misuse (drugs or alcohol)
- Any contact with the criminal justice system
- The need for hepatitis B and C or HIV testing (see relevant recommendations under "Managing Latent TB in Adults" and "Managing Latent TB in Children and Young People" above)
- HIV status
- Other health conditions (physical or mental)
- Communication factors (for example, language and literacy levels)
- Ability to access treatment (mobility and transport needs)
- Employment or entitlement to benefits
- Legal or immigration status (including risk of removal or relocation within the UK)
- Any enablers or incentives to overcome anything that is stopping diagnosis or treatment [2012, amended 2016]

The health and social care plan should:

- State who will be observing treatment and where (if the person is having directly observed therapy this should be provided at a location that is convenient and accessible to them, for example, at a methadone clinic) [2012, amended 2016]
- Include actions to take if contact with the person is lost (for example, keeping details of people who might be able to help re-establish contact) [2012]
- Refer to, and be coordinated with, any other care plan already established for the person [2012]
- Define the support needed to address any unmet health and social care needs (for example, support to gain housing or other benefits, or to help them access other health or social care services) [2012, amended 2016]
- Include a commitment from the person to complete their TB treatment [2012, amended 2016]
- Be supported by frequent contact with any key workers who work with the person [2006 amended 2011, amended 2016]

Multidisciplinary TB teams should aim to find people with active TB who are lost to follow-up, or who stop using services before completing diagnostic investigations. They should report all those lost to follow-up to local Public Health England teams, GPs, the referring organisation and specialist outreach teams. [2012]

Other Strategies to Encourage People to Follow Their Treatment Plan

To encourage people to follow their treatment plan, involve people in treatment decisions for active or latent TB from the start. Emphasise the importance of following the treatment plan when agreeing the regimen. [2016]

Multidisciplinary TB teams should implement strategies for active and latent TB to encourage people to follow the treatment plan and prevent people stopping treatment early. These could include:

- Reminder letters, printed information, telephone calls, texts and apps using an appropriate language [2006, amended 2016]
- Health education counselling and patient-centred interviews [2006, amended 2016]
- Tailored health education booklets from quality sources (see "Providing Information for the Public about TB" above) [2006, amended 2016]
- Home visits [2006]
- Random urine tests and other monitoring (for example, pill counts) [2006]
- Access to free TB treatment for everyone (irrespective of eligibility for other NHS care) and information about help with paying for prescriptions [2006, 2012, amended 2016]
- Social and psychological support (including cultural case management and broader social support) [new 2016]
- Advice and support for parents and carers [new 2016]
- Incentives and enablers to help people follow their treatment regimen [new 2016]

TB control boards should ensure services take into account the barriers facing vulnerable migrants who may need treatment, and in particular the stigma they may face. Other issues include the location of services (both geographically and in terms of opening times) and people's language and cultural needs, in terms of the format of advice and the type of information given. [2012, amended 2016]

Strategies in Prisons or Immigration Removal Centres

On arrival at a prison or immigration removal centre, healthcare professionals should ask all prisoners and detainees (including those being transferred from other establishments) if they are taking TB medication, to ensure continuity of treatment. [2012]

All prisoners and immigration removal centre detainees having treatment for active TB should have a named TB case manager. The case manager should be responsible for contingency planning for discharge from prison or detention. [2012]

Prisons and immigration removal centres should ensure multidisciplinary TB staff have access to prisoners and detainees who need treatment (for example, by being given security clearance). [2012]

All prisoners having treatment for active TB should have directly observed therapy. [2012]

Prison health services should have contingency, liaison and handover arrangements to ensure continuity of care before any prisoner on TB treatment is transferred between prisons or released. In addition, other agencies working with prisoners or detainees should also be involved in this planning. [2012]

Prison and immigration removal centre healthcare services should liaise with the named TB case manager (from the multidisciplinary TB team) to ensure contingency plans for continuation of treatment are drawn up for prisoners and immigration removal centre detainees with TB. [2012]

Multidisciplinary TB teams should ensure accommodation is available for the duration of TB treatment after the prisoner or detainee's release (see "Identifying and Managing Active TB in Prisons, Custody Suites or Immigration Removal Centres: Organisational Factors" below). [2012]

Multidisciplinary TB teams should ensure directly observed therapy is arranged for prisoners or detainees being treated for TB after their release. This should be available close to where they will live in the community. [2012]

Re-establishing Treatment for Active or Latent TB after Interruptions Because of Adverse Events

In people who have experienced a treatment interruption because of drug-induced hepatotoxicity:

- Investigate other causes of acute liver reactions and
- Wait until aspartate or alanine transaminase levels fall below twice the upper limit of normal, bilirubin levels return to the normal range and hepatotoxic symptoms have resolved then
- Sequentially reintroduce each of the anti-TB drugs at full dose over a period of no more than 10 days, starting with ethambutol and either isoniazid (with pyridoxine) or rifampicin [new 2016]

In people with severe or highly infectious TB who need to interrupt standard therapy because of a reaction, consider continuing treatment:

- For hepatotoxicity, a combination of at least 2 anti-TB drugs of low hepatotoxicity (such as ethambutol and streptomycin, with or without a quinolone, such as levofloxacin or moxifloxacin) and monitor with a liver specialist for further reactions
- For a cutaneous reaction, a combination of at least 2 anti-TB drugs with a low risk of cutaneous reactions (such as ethambutol and streptomycin) and monitor with a dermatologist for further reactions [new 2016]

If another reaction of a similar or greater severity occurs because of reintroducing a particular drug, do not give that drug in future regimens and consider extending the total regimen accordingly. [new 2016]

Follow-Up after Treatment Completion

Follow-up clinic visits should not be conducted routinely after treatment completion. [2006]

Tell patients to watch for symptoms of relapse and how to contact the TB service rapidly through primary care or a TB clinic. Key workers should ensure that patients at increased risk of relapse are particularly well informed about symptoms. [2006]

Patients who have had drug-resistant TB should be considered for follow-up for 12 months after completing treatment. Patients who have had multidrug-resistant TB should be considered for prolonged follow-up. [2006]

Service Organisation

Note: When using the recommendations in this section with under-served groups, also check relevant recommendations under "Preventing TB," "Latent TB," "Case Finding," and "Adherence, Treatment Complete and Follow-up" above.

Strategic Oversight and Commissioning of TB Prevention and Control Activities

Public Health England, in partnership with NHS England, should take responsibility for national oversight of TB prevention and control activities. This includes setting up TB control boards (see "Developing the TB Prevention and Control Programme" below). [2012, amended 2016]

Public Health England and NHS England should consider working together to establish control boards in agreed geographical areas and employ appropriate staff (see the recommendation under "Developing the TB Prevention and Control Programme" below). [new 2016]

Clinical commissioning groups and local authority public health teams working in partnership with Public Health England and NHS England should consider collaborative commissioning arrangements through TB control boards. This could, for example, include working with 1 or more clinical commissioning groups to cover a major metropolitan district, region or TB control board area taking into account:

- Local TB incidence
- Local at-risk populations and their movements across different geographical areas
- Existing service configurations for organisations involved in TB prevention and control
- The need to share services, such as mobile X-ray facilities, and outreach incident teams across different geographical areas [2012, amended 2016]

TB control boards should develop TB prevention and control programmes working with commissioners, Public Health England and NHS England. The board could include clinical, commissioning (from clinical commissioning groups, local government and the voluntary sector) and public health leaders and people with TB or groups who advocate on their behalf from across the control board area. This may include identifying a lead clinical commissioning group, which could be led by an executive director of that commissioning group working with the board. Feedback mechanisms between local commissioning groups and the TB control board should be developed. [new 2016]

An executive director of local commissioning groups, working with the local director of public health or another nominated public health consultant, should lead implementation of the programme in their locality. The lead should ensure a comprehensive prevention and control programme is commissioned to support the level of need (see "Local Needs Assessment" below) and that they work with the control board regularly. [2012, amended 2016]

Working together through TB control boards and local networks, commissioners, local government and Public Health England should ensure TB prevention and control programmes set up multidisciplinary TB teams to provide all TB services (see "Commissioning Multidisciplinary TB Support" below). They should ensure that local strategy and service commissioning focuses on an end-to-end pathway. [2012, amended 2016]

Working together through TB control boards, commissioners and Public Health England should ensure the TB prevention and control programme is informed by relevant NICE guidance and developed in collaboration with clinical services. It should also be informed by the standard minimum

data set collected through local needs assessment and service audit. [2012, amended 2016]

Working together through TB control boards, commissioners and Public Health England should ensure the TB prevention and control programme targets all ages, including children, and covers all aspects of TB prevention and control (see recommendations under "Developing the TB Prevention and Control Programme" below), including but not limited to:

- Active case finding (contact investigations and identifying latent TB in high-risk groups)
- Awareness-raising activities
- Standard and enhanced case management (including providing directly observed therapy and free treatment)
- Finding people lost to follow-up and encouraging them back into treatment
- Incident and outbreak control
- Monitoring, evaluating and gathering surveillance and outcome data [2012, amended 2016]

Working together through TB control boards, commissioners, Public Health England and the voluntary sector should ensure TB prevention and control programmes take account of the need to work with other programmes targeting specific high-risk groups, such as those who are under-served. Examples include programmes focused on the health of asylum seekers and refugees, underserved children, homelessness and housing, offenders and people who misuse substances. [2012, amended 2016]

TB control boards should consider integrating TB and HIV services, joint clinics and training opportunities. [new 2016]

Commissioners should consider commissioning support and advice to all groups diagnosed with TB irrespective of whether they are under-served. [new 2016]

Developing the TB Prevention and Control Programme

TB control boards should be responsible for developing a TB prevention and control programme based on the national strategy and evidence-based models. [new 2016]

TB control boards should plan, oversee, support and monitor local TB control, including clinical and public health services and workforce planning. [new 2016]

TB control boards should assess services in their area, identify gaps in provision and develop plans to meet these, including:

- Undertaking a workforce review to support local or regional commissioning of TB services to meet the needs of their population (see "Local Needs Assessment" and "Cohort Review" below)
- Supporting development of appropriate services and pathways to improve access and early diagnosis (see "Rapid-Access Radiology and Other Investigation Results – Referral to Multidisciplinary TB Team Process" above and "Non-clinical Roles Including TB Support Workers" and "Rapid-Access TB Services" below)
- Negotiating arrangements to cover the cost of additional services to address specific gaps in current TB control arrangements [new 2016]

TB control boards should ensure cohort review is undertaken at least quarterly, and the results are fed back to local clinical and TB networks. These should be agreed by accountable bodies such as clinical commissioning groups, trust management, regional Public Health England and centre directors and local authority directors of public health as agreed, all of whom should make sure appropriate action is taken. [new 2016]

TB control boards should enable full and consistent use of national guidelines including:

- Ensuring the needs of all people with TB, particularly under-served populations, are addressed
- Ensuring contact tracing arrangements are appropriate to the needs of the population (see "Case Finding" above)
- Assuring themselves that TB control in low-incidence areas is established and delivered appropriately (see "Rural Services: Organisational and Support Factors" below)
- Assuring themselves that multidrug-resistant TB is managed appropriately (see "Multidrug-Resistant TB" above) and mechanisms are in place to ensure:
    - There is sufficient clinical expertise available to manage cases
    - Regional multidrug-resistant TB networks take account of expert advice (see "Regional Multidrug-Resistant TB Network" below) [new 2016]

TB control boards should develop links and partnerships and establish agreed relationships and lines of accountability between TB control boards and local clinical and TB networks. This includes engaging with other key stakeholders to ensure universal coverage of TB control efforts. [new 2016]

TB control boards should collaborate with their local and regional partners. They should agree and establish regular monitoring, surveillance and reporting arrangements with all partners to support needs assessment (see "Local Needs Assessment" below) and regular audit and evaluation. [new 2016]

TB control board staff should have clearly defined roles and responsibilities. Their roles and responsibilities could include:

- Establishing the links, partnerships and relationships between all aspects of the control board area within their remit (if necessary across usual geographical commissioning boundaries)
- Developing and supporting adoption and implementation of evidence-based model service specifications for the clinical and public health actions needed to control TB including:
    - Improving access and early diagnosis (see "Raising and Sustaining Awareness of TB," "Providing Information for the Public about TB," and " Rapid-Access Radiology and Other Investigation Results – Referral to Multidisciplinary TB Team Process" above and "Non-clinical Roles Including TB Support Workers" below)
    - Diagnostics, treatment and care services (see "Latent TB" and "Active TB" above)
    - Contact investigations and tracing (see "Diagnosing Latent TB in Adults" and "Contact Tracing" above)
    - Cohort review (see "Cohort Review" below)
    - Vaccination (see "BCG Vaccination" above)
    - Drug resistance (see "Multidrug-Resistant TB" above)
    - Tackling TB in under-served populations
    - Surveillance, monitoring and quality assurance
    - Workforce development and commissioning (see "Commissioning Multidisciplinary TB Support" and "Non-clinical Roles Including TB Support Workers" below) [new 2016]

TB control boards should ensure there is sufficient capacity available to them to manage a sudden increase in demand such as:

- TB contact investigations, (such as incidents in congregate settings)
- Large scale active case-finding initiatives in under-served groups in the community
- Outbreaks in a variety of settings or sites where transmission risk may be high, including but not limited to schools, workplaces, hostels and prisons [new 2016]

To set up, monitor and evaluate a TB control programme, TB control boards should:

- Agree plans within their partnerships to assess local services against the service specifications
- Develop plans and quality standards to secure improvements
- Establish quality assurance mechanisms and regular audits including, but not limited to, cohort review for all aspects of the TB control board partnership plans [new 2016]

Coordinating Local TB Networks

TB control boards should (in collaboration with commissioners) consider the need for a TB network local coordinator, particularly if working across multiple clinical commissioning group areas (see recommendation under "Strategic Oversight and Commissioning of TB Prevention and Control Activities" above). [new 2016]

The coordinator should work in close collaboration with clinicians and all relevant multidisciplinary TB teams to develop the network and be responsible for:

- Setting up the network and developing it based on needs, reporting back to the TB control board regularly
- Establishing the links, partnerships and relationships across their local network (if necessary across usual geographical commissioning boundaries) [new 2016]

Regional Multidrug-Resistant TB Network

TB control boards should consider setting up a regional multidisciplinary TB network to oversee management of multidrug-resistant TB. This could:

- Identify and designate regional expert centres
- Ensure all healthcare professionals who suspect or treat a case of multidrug-resistant TB are informed about and have access to specialist advisory services for multidrug-resistant TB. This includes the designated expert centre in their regional network and may also include the national advisory service for multidrug-resistant TB (currently provided by the British Thoracic Society).
- Ensure all cases of multidrug-resistant TB are discussed at the regional multidisciplinary TB team meeting in the local clinical network

- Formally consider and record the advice from the specialist advisory services for multidrug-resistant TB provided by the designated regional expert centre or the national advisory service for multidrug-resistant TB [new 2016]

Rural Services: Organisational and Support Factors

Commissioners in rural areas (working with the TB control board) should consider collaborative approaches to deliver and manage TB services. They could, for example, set up a network including areas with high and low incidence of TB. [new 2016]

Local Needs Assessment

Directors of public health, in discussion with local health protection teams, should ensure that TB is part of the joint strategic needs assessment. [2012, amended 2016]

Directors of public health should provide commissioners of TB prevention and control programmes and TB control boards with local needs assessment information annually using data provided by Public Health England. [2012, amended 2016]

Commissioners of TB prevention and control programmes should ensure services reflect the needs of their area, identified by needs assessment. Health and wellbeing boards should ensure that local TB services have been commissioned based on local needs identified through needs assessment. [2012, amended 2016]

Directors of public health and TB control boards should use cohort review (see "Cohort Review" below) and other methods to collect data on the following, to inform local needs assessment:

- Number of annual notified TB cases (see Public Health England's enhanced TB surveillance data and annual 'suite of indicators')
- Size, composition (for example, age and ethnicity) and distribution of local at-risk groups
- Indices of social deprivation
- Local statutory and non-statutory services working with these groups
- Organisation of local TB services, including the composition and capacity of the local multidisciplinary TB team (see the results of local audit) and location of services. This may also include data to support evaluating the need for integrated TB/HIV services including joint clinics.
- Numbers needing enhanced case management (see "Adherence, Treatment Completion and Follow-up" above)
- Numbers receiving directly observed therapy from the start of, or at any point during, treatment (see Public Health England's enhanced TB surveillance data).
- Evidence of recent transmission (for example, using DNA fingerprinting or surrogate markers such as number of cases in children under 5 years (see UK TB strain-typing database and local incident and outbreak reports)
- Completeness and yield of contact investigations. This includes: proportion of smear-positive cases with 0, 5 or more contacts identified; proportion of identified contacts clinically assessed; and proportion of contacts with latent TB infection who successfully complete treatment.
- Active case-finding initiatives, incident contact investigations and identification of latent TB infection in high-risk groups
- Treatment outcomes for everyone grouped according to social risk factors and by the use of directly observed therapy (including rates of loss to follow-up and treatment interruptions – see Public Health England's enhanced TB surveillance data)
- Local education and awareness-raising programmes for under-served groups, professionals and practitioners working with them
- Views and experiences of people with TB, carers and the services working with them [2012, amended 2016]

Local needs assessments should also be equity proofed to assess the potential effect of planning, commissioning and policy decisions on health inequalities (see planning and commissioning services in NICE's local government briefing on health inequalities and population health). [new 2016]

Cohort Review

TB control boards and prevention and control programme leads should initiate, audit and evaluate cohort reviews in their commissioning area. Quarterly cohort review meetings should take place in the area covered by the programme. Combine these meetings with others if possible, or use technology to make it easier for clinicians and case managers to attend. [2012, amended 2016]

TB case managers should present standardised information on each case, including: demographic information, HIV test results, pre-treatment and ongoing status (clinical, laboratory, radiology), adherence to treatment and the results of contact investigations. [2012, amended 2016]

TB case managers and key allied professionals from the TB prevention and control programme should attend cohort review meetings. This could

include the lead clinician (who may or may not be the case manager). Either a paediatrician with experience and training in the treatment of TB or a general paediatrician with advice from a specialised clinician should be present when cases of children with TB are presented. [2012, amended 2016]

The chair of the cohort review should not work for any of the TB services included in the review. Examples of possible chairs include a public health consultant, a specialist physician or a senior TB nurse, preferably from a different geographical area. Alternatively the chair could be a representative from the local Public Health England health protection team or the TB control board. [2012, amended 2016]

Multidisciplinary TB teams, in conjunction with Public Health England units, should collate and present cohort review data on TB treatment and the outcome of contact investigations at the review meetings. In addition, progress towards national, regional and local service targets should be presented. [2012, amended 2016]

TB control boards, directors of public health and local public health consultants should ensure outputs from the cohort review feed into the needs assessment for TB services. TB control board directors should attend the cohort review at least once a year. [2012, amended 2016]

TB case managers should provide feedback promptly to multidisciplinary TB teams on issues identified as a result of cohort review. The results of the cohort review should be collated locally and agreed by the chair before being fed back to TB control boards, commissioners and health and wellbeing boards regularly and via needs assessment. [2012, amended 2016]

People participating in a cohort review should review the results and evaluate local services (for example, auditing adverse outcomes, rates of culture confirmation, treatment completion rates or time to diagnosis). [2012, amended 2016]

Commissioning Multidisciplinary TB Support

Commissioners should ensure multidisciplinary TB teams:

- Have the skills and resources to manage the care of people with active TB who are not from under-served groups. [2012, amended 2016]
- Include at least 1 TB case manager with responsibility for planning and coordinating the care of under-served people and those with active TB who receive enhanced case management. [2012, amended 2016]
- Have the resources to manage latent TB care in under-served groups and the wider population. [new 2016]
- Include a range of clinical specialties in the multidisciplinary TB team, including paediatrics, infection control and respiratory medicine. [2012]
- Have regular attendance at these multidisciplinary team and cohort review meetings for all team members included as a programmed activity as part of their work planning. [new 2016]
- Have the skills and resources necessary to manage the care of people with complex social and clinical needs (either directly or via an established route). This includes the ability to provide prompt access (or if necessary, referral) to skilled outreach and advocacy workers who can draw on the services of allied practitioners. The aim is to address people's housing, asylum, immigration, welfare, substance dependency and other health and social care needs. (The allied practitioner support should include both a specified housing officer and a social worker.) [2012]
- Can provide rapid access TB clinics for all cases, including under-served groups. [2012]
- Consider providing administration support for TB nurses and case managers so they have capacity for clinical and case management work. This could include giving TB nurses access to computer hardware and software. [new 2016]
- Have the resources to provide a continuous service throughout the year, ensuring the TB service accounts for the following to manage continuity of care:
    - Planned absence (for example, professional development, mandatory training, annual, maternity or paternity leave)
    - Unplanned absence (such as sickness absence) [2012, amended 2016]
- Can provide prompt access to a professional who has training and experience in assessing and protecting children and vulnerable adults at risk of abuse or neglect. [2012]
- Have access to funds through local government and clinical commissioning groups that can be used flexibly to improve adherence to treatment among under-served groups. For example, funds could be used to provide transport to clinics, to provide support or enablers for treatment, or for paying outreach workers or community services to support directly observed therapy. Funds may also be used to provide accommodation during treatment (see "Accommodation during Treatment" below). [2012, amended 2016]
- Have the resources to provide ongoing TB awareness-raising activities for professional, community and voluntary (including advocacy) groups that work with populations at high risk of TB (see "Raising and Sustaining Awareness of TB" above). These resources could be financed by local government or clinical commissioning groups. [2012, amended 2016]

Commissioners should ensure NHS England's safe staffing principles are applied when commissioning TB services[2,3]. [new 2016]

Non-Clinical Roles Including TB Support Workers

TB control boards and local TB services should consider employing trained, non-clinically qualified professionals to work alongside clinical teams to agreed protocols, and to contribute to a variety of activities. Examples of this may include awareness raising and supporting people to attend appointments (including other health and social care appointments). They could also help with collecting samples, contact tracing, case management including directly observed therapy and cohort review, or any other aspect of the service if:

- They are trained to deliver the intervention or processes effectively
- They are supported, mentored and supervised by a named case manager, such as a TB nurse
- They have the skills to monitor, evaluate and report on their work practices and outcomes to maintain a process of ongoing evaluation and service improvement in relation to cohort review (see "Cohort Review" above) [new 2016]

TB control boards should ensure that people working in the TB service have the right knowledge, engagement, advocacy and communication skills to meet the needs (for example, language, cultural or other requirements) of all the groups they may work with. [new 2016]

Commissioners should consider taking into account different needs across traditional geographical and organisational boundaries. Put agreements in place so that staff can work across these boundaries, covering the whole service or TB control board area if appropriate. [new 2016]

Commissioners and TB control boards should ensure they put in place appropriate governance (including clear lines of accountability and extension of scope of practice) and data sharing practices and agreements. This includes ensuring they are part of service level agreements between NHS and non-NHS services, for example, the third sector or local government, and appropriate training has been completed. [new 2016]

Rapid-Access TB Services

Multidisciplinary TB teams should establish relationships with statutory, community and voluntary organisations that work with people at risk of TB to develop appropriate TB referral pathways. They should ensure these organisations know how to refer people to local TB services. [2012]

Multidisciplinary TB teams should accept referrals from healthcare providers and allied organisations working in the community with under-served groups. This includes voluntary and statutory organisations (for example, mobile X-ray teams or community organisations or outreach workers working with vulnerable migrants). [2012]

Multidisciplinary TB teams should accept self-referrals to TB clinics by people who suspect they have TB or have recently been in contact with someone with TB. [2012, amended 2016]

Multidisciplinary TB teams should consider accepting direct referrals from emergency departments (see "Rapid-Access Radiology and Other Investigation Results – Referral to Multidisciplinary TB Team Process" above). [new 2016]

Healthcare professionals should consider urgent referral to TB clinics for people with suspected active TB. They should also ensure the results from first-line diagnostic tests (including a sputum smear and chest X-ray) are available before the person sees a specialist. (Note: this should not delay the referral.) [2012, amended 2016]

Multidisciplinary TB teams should have pathways to triage referrals, start investigations and collect clinical information before the person is seen by a physician. [new 2016]

While triaging, multidisciplinary TB teams should ensure everyone is given information about TB as part of the process (see "Providing Information for the Public about TB" above). This should include who the person should contact if they have any questions and how to access advice or information from support groups, national charities such as TB Alert and other sources such as local government (for example, public health or social care teams). [2016]

Multidisciplinary TB teams should ensure people who have a smear-positive result or imaging features highly suggestive of smear-positive TB (for example, evidence of cavitation on chest X-ray) are assessed the next working day. This is so that case management and infection control procedures start promptly. [2012, amended 2016]

The multidisciplinary TB team should assess people who are not smear-positive but have imaging that suggests pulmonary or laryngeal TB as soon as possible. This should be no later than 5 working days after a referral. [2012, amended 2016]

Multidisciplinary TB teams should, where necessary, be able to provide or arrange outreach services to ensure sputum samples or other assessments such as contact investigations can be arranged in the community. [2016]

Identifying and Managing Active TB in Prisons, Custody Suites or Immigration Removal Centres: Organisational Factors

Multidisciplinary TB teams, prisons, custody suites and immigration removal centre healthcare services should have named TB liaison leads to ensure they can communicate effectively with each other. [2012, amended 2016]

Prison, custody suites and immigration removal centre healthcare services should develop a TB policy by working with the TB control board and multidisciplinary TB team and the local Public Health England health protection team. [2012, amended 2016]

Multidisciplinary TB teams, in conjunction with prisons, custody suites and immigration removal centre healthcare services, should agree a care pathway for TB. This is to ensure that any suspected or confirmed cases are reported to, and managed by, the multidisciplinary TB team. [2012, amended 2016]

Multidisciplinary TB teams, in liaison with prisons, custody suites or immigration removal centre healthcare providers, should manage all cases of active TB. Investigations and follow-up should be undertaken within the prison or immigration removal centre if possible. [2012, amended 2016]

Accommodation During Treatment

Multidisciplinary TB teams should assess the living circumstances of people with TB. Where there is a housing need they should work with allied agencies to ensure that all those who are entitled to state-funded accommodation receive it as early as possible during their treatment, for example, as a result of a statutory homelessness review and identified need. [2012, amended 2016]

Multidisciplinary TB teams, commissioners, local authority housing lead officers and other social landlords, providers of hostel accommodation, hospital discharge teams, Public Health England and the Local Government Association should work together to agree a process for identifying and providing accommodation for homeless people diagnosed with active pulmonary TB who are otherwise ineligible for state-funded accommodation. This includes people who are not sleeping rough but do not have access to housing or recourse to public funds. The process should detail the person's eligibility and ensure they are given accommodation for the duration of their TB treatment. [2012, amended 2016]

Local government and clinical commissioning groups should fund accommodation for homeless people diagnosed with active TB who are otherwise ineligible for state-funded accommodation. Use health and public health resources, in line with the Care Act 2014 . [2012, amended 2016]

Multidisciplinary TB teams should make people who would not otherwise be entitled to state-funded accommodation aware that they may lose this accommodation if they do not comply with treatment. They should ensure plans are made to continue housing people once their TB treatment is completed. [2012]

Public Health England, working with the Local Government Association and their special interest groups, should consider working with national housing organisations such as the Chartered Institute of Housing , Homeless Link , Sitra and the National Housing Federation to raise the profile of TB. This is to ensure people with TB are considered a priority for housing. [new 2016]

Consider training housing commissioners and frontline staff on TB and the need for housing support, so that they understand that a stable home life is a prerequisite to successful TB treatment. [new 2016]

Footnotes

[1]At the time of publication (January 2016) the BNF states: 'The Mantoux test is recommended for tuberculin skin testing, but no licensed preparation is currently available. Guidance for healthcare professionals is available at www.dh.gov.uk/immunisation .'

[2]The staffing ratios used in Public Health England and NHS England's collaborative tuberculosis strategy for England (published in 2015) came from NICE's guideline on tuberculosis: identification and management in under-served groups (published in 2012) which has been replaced by this guideline.

[3]NICE's 2012 guideline on tuberculosis: identification and management in under-served groups recommended 1 WTE case manager per 40 incident cases needing standard management and 1 WTE case manager per 20 incident cases needing enhanced case management.

Definitions

Strength of Recommendations

Some recommendations can be made with more certainty than others. The Guideline Development Group (GDG) makes a recommendation based on the trade-off between the benefits and harms of an intervention, taking into account the quality of the underpinning evidence. For some interventions, the GDG is confident that, given the information it has looked at, most patients would choose the intervention. The wording used in the recommendations in this guideline denotes the certainty with which the recommendation is made (the strength of the recommendation).

Interventions That Must (or Must Not) Be Used

The GDG usually uses 'must' or 'must not' only if there is a legal duty to apply the recommendation. Occasionally the GDG uses 'must' (or 'must not') if the consequences of not following the recommendation could be extremely serious or potentially life threatening.

Interventions That Should (or Should Not) Be Used – a 'Strong' Recommendation

The GDG uses 'offer' (and similar words such as 'refer' or 'advise') when confident that, for the vast majority of patients, an intervention will do more good than harm, and be cost effective. Similar forms of words (for example, 'Do not offer…') are used when the GDG is confident that an intervention will not be of benefit for most patients.

Interventions That Could Be Used

The GDG uses 'consider' when confident that an intervention will do more good than harm for most patients, and be cost effective, but other options may be similarly cost effective. The choice of intervention, and whether or not to have the intervention at all, is more likely to depend on the patient's values and preferences than for a strong recommendation, and so the healthcare professional should spend more time considering and discussing the options with the patient.

Recommendation Wording in Guideline Updates

NICE began using this approach to denote the strength of recommendations in guidelines that started development after publication of the 2009 version of 'The guidelines manual' (January 2009). This does not apply to any recommendations ending [2006], [2011] and [2012]. In particular, for recommendations labelled [2006] and [2012], the word 'consider' may not necessarily be used to denote the strength of the recommendation.

Clinical Algorithm(s)

A National Institute for Health and Care Excellence (NICE) pathway titled "Tuberculosis overview" is provided on the NICE Web site .

Scope

Disease/Condition(s)

Tuberculosis (TB), including latent, active, and multi-drug resistant TB infection

Other Disease/Condition(s) Addressed

Human immunodeficiency virus (HIV)

Guideline Category

Diagnosis

Management

Prevention

Risk Assessment

Screening

Treatment

Clinical Specialty

Family Practice

Infectious Diseases

Internal Medicine

Pediatrics

Preventive Medicine

Pulmonary Medicine

Intended Users

Advanced Practice Nurses

Allied Health Personnel

Health Care Providers

Nurses

Patients

Pharmacists

Physician Assistants

Physicians

Public Health Departments

Social Workers

Substance Use Disorders Treatment Providers

Guideline Objective(s)

- To update recommendations on the prevention, diagnosis and management of latent and active tuberculosis (TB), including both drug susceptible and drug resistant forms of the disease
- To review the organisation of relevant TB services as it relates to activities undertaken in any setting in which National Health Service (NHS) or public health services for TB are received, provided or commissioned in the public, private and voluntary sectors

Target Population

- Adults, young people and children who have, or who are suspected to have, active tuberculosis (TB) caused by *Mycobacterium tuberculosis* complex (*M. tuberculosis*, *M. africanum*, *M. bovis*)
- Adults, young people and children who have latent infection with *M. tuberculosis* complex, but not active disease
- Adults, young people and children at increased risk of infection with *M. tuberculosis* complex and/or at increased risk of progressing to the active disease

Interventions and Practices Considered

Diagnosis

1. Diagnosing latent tuberculosis (TB)
    - Mantoux testing
    - Interferon gamma-release assay
2. Diagnosing active pulmonary or laryngeal TB

- Clinical signs or symptoms
- Tests, including chest X-ray, nucleic acid amplification test, microscopy, histology, cultures, interferon gamma-release assay (paediatric population)
- Respiratory samples

3. Diagnosing active extrapulmonary TB
    - Clinical signs or symptoms
    - Tests, including chest X-ray, nucleic acid amplification test, microscopy, histology, cultures

Management/Treatment/Prevention

1. Prevention
    - Prevention in healthcare environments: new employees and occupational health
    - Prevention in prisons and remand centres
    - Infection control, including isolation
    - Bacille Calmette-Guerin (BCG) vaccination by population (neonates, infants and older children, new entrants from high-incidence countries, healthcare workers, contact of people with active TB, other groups)
    - Strategies to increase uptake of BCG vaccination
2. Management of latent TB
    - Criteria for recipients of treatment for latent TB infection
    - Treatment of latent TB (isoniazid)
    - Management of liver function
    - Testing for human immunodeficiency virus (HIV) infection, hepatitis B, and hepatitis C
3. Management of active TB
    - Combination medicines (isoniazid with pyridoxine, rifampicin, pyrazinamide, ethambutol)
    - Dosing schedule and duration of treatment
    - Use of adjunctive corticosteroids
    - Use of adjunctive surgery
    - Treatment of active TB in people with comorbidities and coexisting conditions (HIV infection, liver disease, renal disease, diabetes, substance misuse, impaired vision or eye disease, pregnancy or breastfeeding)
    - Treatment interruptions
    - Treatment completion and follow-up
4. Management of drug-resistant TB
    - Assessment of risk factors for drug resistance
    - Identifying drug resistance
    - Referral
    - Drug treatment (excluding multidrug- and extensively drug-resistant TB)
5. Adherence
    - Identifying and managing TB among hard-to-reach groups
    - Ensuring adherence and treatment completion
    - Raising awareness and the provision of information to the public (information, education, and support)
    - Involving patients in decisions about prescribed medications
6. Service organisation
    - Identifying and managing TB among hard-to-reach groups
    - Organisation and delivery of TB services
7. Active case finding
    - Contact tracing (human-to-human transmission, cases on aircraft, cases in schools, cases in community childcare, cases in hospital inpatients)
    - Case finding in street homeless people

Major Outcomes Considered

- Diagnosis
    - Diagnostic utility and accuracy
    - Time to diagnosis or treatment initiation

    - Prognostic value of tests
    - Acceptability of approach
    - Adverse events
    - Health-related quality of life
    - Resource use and cost
- Treatment
    - Mortality
    - Adverse events
    - Adherence and treatment completion
    - Treatment success and rate of recovery, or treatment failure, relapse and emergence of drug resistance
    - Health-related quality of life
    - Resource use and cost
- Infection control
    - Tuberculosis (TB) transmission rate
    - Acceptability of approach
    - Health-related quality of life
    - Resource use and cost
- Promoting the uptake of, and improving adherence to, treatment
    - Uptake and completion of treatment
    - Acceptability of approach
    - Direct and indirect measures of adherence (for example, direct observation of people taking their medication and self-reported medication taking)
    - Barriers to uptake and adherence to treatment
- Bacille Calmette-Guerin (BCG) vaccination uptake in at-risk groups
    - Uptake of BCG vaccination
    - Barriers to uptake
- Information, education and support
    - Knowledge and awareness of TB among people who have, or who are at high-risk from TB and relevant staff, including how to recognise symptoms, the need for rapid diagnosis, referral and access to specialist TB services, and the need for prompt, complete treatment
    - Health, social and economic outcomes for people affected by TB

Methodology

Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Hand-searches of Published Literature (Secondary Sources)

Searches of Electronic Databases

Searches of Unpublished Data

Description of Methods Used to Collect/Select the Evidence

Note from the National Guideline Clearinghouse (NGC): This guideline was developed by the Internal Clinical Guidelines Team on behalf of the National Institute for Health and Care Excellence (NICE). See the "Availability of Companion Documents" field for the full version of this guidance and related appendices, including methodology used for previous versions of the guideline.

Clinical Sections

Developing Review Questions and Protocols

The technical team drafted review questions during the scoping process (see final scope in Appendix B) which were refined and validated by the Guideline Development Group (GDG), using a Population, Intervention, Comparator, Outcome (PICO) framework. The GDG and technical team jointly prepared a protocol for each review question (see Appendix C). These protocols formed the starting point for systematic reviews of relevant evidence.

Identifying the Evidence

Published evidence was identified by applying systematic search strategies (see Appendix C) to the following databases: Medline (1950 onwards), EMBASE (1980 onwards), Cumulative Index to Nursing and Allied Health Literature (CINAHL; 1982 onwards), and three Cochrane databases (Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews, and the Database of Abstracts of Reviews of Effects). Searches to identify economic studies were undertaken using the above databases, the National Health Service Economic Evaluation Database (NHS EED) and the Health Technology Assessment (HTA) database.

Where a question was updated directly from the previous version of the guideline, the search strategies used in that guideline were updated. No date restrictions were placed on the searches for all new questions.

Searches in EMBASE and Medline were limited to English language and studies in humans. None of the other searches were limited by language of publication (although publications in languages other than English were not reviewed). Validated search filters were used to identify particular study designs, such as randomised controlled trials (RCTs). There was no systematic attempt to search grey literature (conference abstracts, theses or unpublished trials), nor was hand searching undertaken of journals not indexed on the databases.

Towards the end of the guideline development process, the searches were updated and re-executed to include evidence published and indexed in the databases by 2nd December 2014.

Reviewing Process

Study Identification

All titles and abstracts identified by the literature searches were sifted for relevance and data were extracted by 1 reviewer. A second reviewer checked a random 10% of sifted out titles and abstracts for accuracy.

When full text articles were ordered and obtained, 1 reviewer examined each article against the inclusion criteria specified in the review protocol and decided if the study should be included or excluded. All excluded studies and the reason for exclusion and all extracted data from included studies were checked by a second reviewer and the GDG.

Health Economics

Literature reviews seeking to identify published cost–utility analyses of relevance to the issues under consideration were conducted for all questions. In each case, the search undertaken for the clinical review was modified, retaining population and intervention descriptors, but removing any study-design filter and adding a filter designed to identify relevant health economic analyses. Search strategies are provided in full in Appendix C. In assessing studies for inclusion, population, intervention and comparator, criteria were always identical to those used in the parallel clinical search; only cost–utility analyses were included. Economic evidence profiles, including critical appraisal according to the Guidelines manual (see the "Availability of Companion Documents" field), were completed for included studies; these are shown in Appendix F.

Economic studies identified through a systematic search of the literature are appraised using a methodology checklist designed for economic evaluations (NICE 2012; see Appendix F). This checklist is not intended to judge the quality of a study per se, but to determine whether an existing economic evaluation is useful to inform the decision-making of the GDG for a specific topic within the guideline.

Service Delivery Section

A systematic review was conducted on the organisation and delivery of TB services, in accordance with the NICE Interim methods guide for developing service guidance (February 2013). The areas of interest were identified by the GDG as the UK, New York City, Canada, Barcelona, and the Netherlands. The review was split into three parts: a case study approach, an effectiveness review, and an economic review (see Appendix G7 for the full report, "Evidence Review of TB Service Delivery").

Searching

A comprehensive search strategy was developed involving both a database search (n=5197 after duplicates were removed) and a grey literature search (n=180), for studies published between 2003 and April 2014; see Appendix 1 of the service delivery review for full details of the search methodology.

Alongside the formal searches, a call for evidence among stakeholders was undertaken between March and April 2014, including members of the GDG and Service Delivery Group (SDG) for recommendations on relevant published and unpublished literature, in accordance with the inclusion criteria.

Selection of Studies

The evidence identified via the formal literature searches, grey literature search, and the call for evidence, were compiled and screened for the inclusion of:

- Case studies: a sub-set of descriptive literature to provide the background information on epidemiology, legislation, policy, priorities for action, service models/structures or organisational elements, staff and settings in the case study areas
- Effectiveness review: quantitative study designs that provided estimates of the effectiveness of service models or interventions (including comparative studies, noncomparative studies, or evaluations/audits of TB services)
- Economics review: economic analyses of the cost-effectiveness/impact of service models or interventions (including cost-benefit, cost-effectiveness, cost-utility, modelling studies, or cost-impact analyses)

A service delivery intervention/model was defined as any service adaptation, such as process changes, change in delivery setting or mode (including staff), change in structure, accountability or commissioning of a TB service.

Due to the large volume of studies identified in the formal searches, three separate screening phases were undertaken: a high-level sift at title stage, a title and abstract sift, and a full text screening stage. Screening (stages 1 and 2) of the database searches was undertaken and recorded in an ACCESS database. Stage 3 screening was done at the full paper level, with decisions recorded in the ACCESS database. Screening was undertaken by individual reviewers, with any uncertainties flagged for discussion with a second reviewer. Details of the screening criteria at each stage are available in Appendix 2 of the service delivery report.

Studies from the grey literature and the call for evidence were screened by one reviewer in Microsoft Word. Due to the small volume of studies, screening was undertaken at the full text stage. Included studies were subsequently filtered to:

- Case study background
- Effectiveness review
- Economic review

To ensure that the most recent information was included in the effectiveness and economics review, an update search was conducted on 5th February 2015 for studies published in 2014. Only comparative studies were considered. The case study review was not updated.

The flow of included studies is presented in Figure 1 in the service delivery report. Please note that studies could be identified as fitting more than one category. For example studies could have been identified for inclusion in both the effectiveness and economics reviews, and likewise may have been included in both the effectiveness review and case studies.

Expert Testimony

'Colloquial evidence' was used to complement the scientific evidence or provide missing information on context. It included evidence about values (including political judgement), practical considerations (resources, professional experience or expertise and habits or traditions) and the interests of specific groups (views of lobbyists and pressure groups). Expert testimony was used when:

- Evidence reviews have uncovered significant gaps in the evidence (or the development team is aware from the outset that the formal evidence is likely to be limited)
- The available evidence conflicts significantly
- The SDG wished to seek the views and experiences of specific groups of researchers, practitioners, clients or service users.

Expert testimony was used to provide a range of information about interventions and programmes, including:

- Context – for example, the policy or commissioning context
- Effectiveness – for example, preliminary results from ongoing interventions or services
- Service design and delivery – for example, detailed information on how a particular service is implemented with different groups of people
- Experience – for example, views and experiences of groups of people who have experience of relevant services or practitioners

The SDG received testimony from a number of experts (lay and professional) in the field on a number of topics.

Number of Source Documents

Clinical Sections

The number of source documents for each review question are detailed in the "Evidence Review," "Evidence Statements," and "Health Economic Evidence" sections of the full version of the guideline (see the "Availability of Companion Documents" field).

Service Delivery Section

Details on the number of source documents used for the section on organisation and delivery of tuberculosis (TB) services are provided in Appendix G7 of the full version of the guideline (see the "Availability of Companion Documents" field).

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Overall Quality of Outcome Evidence in Grading of Recommendations Assessment, Development and Evaluation (GRADE)

Level	Description
High	Further research is very unlikely to change confidence in the estimate of effect.
Moderate	Further research is likely to have an important impact on confidence in the estimate of effect and may change the estimate.
Low	Further research is very likely to have an important impact on confidence in the estimate of effect and is likely to change the estimate.
Very Low	Any estimate of effect is very uncertain.

Methods Used to Analyze the Evidence

Meta-Analysis

Review of Published Meta-Analyses

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

Note from the National Guideline Clearinghouse (NGC): This guideline was developed by the Internal Clinical Guidelines Team on behalf of the National Institute for Health and Care Excellence (NICE). See the "Availability of Companion Documents" field for the full version of this guidance and related appendices, including methodology used for previous versions of the guideline.

Clinical Sections

Data Extraction

Basic characteristics of each included study were summarised into standardised evidence tables for each review question (see Appendix D) along with the quality assessment of the evidence. Where outcome data were presented, results were entered as reported in the full-text report of the study. Where data required for analysis were missing, data was imputed as shown in Table 2 of the full version of the guideline.

Quality Assessment Checklists

For randomised controlled trials (RCTs), the NICE methodological checklist for RCTs was used for quality assessment of the evidence. For cohort studies, the NICE methodological checklist for cohort study was used for quality assessment. For diagnostic studies, the Quality Assessment for Diagnostic Studies (QUADAS) checklist was used for quality assessment. For qualitative studies, the Critical Appraisal Skills

Programme (CASP) checklist for qualitative research design was used for quality assessment.

Meta-analyses

Where possible, meta-analyses were conducted to combine the results of studies for each outcome. For continuous outcomes, where change from baseline data were reported in the trials and were accompanied by a measure of spread (for example standard deviation), these were extracted and used in the meta-analysis.

Dichotomous outcomes were presented as odds ratios (ORs), relative risks (RRs) or hazard ratios (HRs) with 95% confidence intervals (CIs). Continuous outcomes were presented as mean differences with 95% CIs or SDs, unless data was reported in a form in which this was not possible (for example, as medians and ranges or interquartile ranges).

Software

Data for intervention reviews were analysed using Review Manager 5.1, data for diagnostic reviews was analysed using STATA or R, and WinBUGS was used for network meta-analyses.

Network Meta-Analysis (NMA) Methods

NMAs were conducted to simultaneously compare multiple treatments in a single meta-analysis, preserving the randomisation of the included trials in the reviews. This allows all evidence to be combined in a single internally consistent model.

An extensive series of NMAs was undertaken to synthesise evidence on pharmacological treatments to treat latent tuberculosis infection.

Hierarchical Bayesian NMA was performed using the software WinBUGS version 1.4.3. The models were based on the approach and code provided in the NICE Decision Support Unit's Technical Support Documents on evidence synthesis, particularly Technical Support Document 2 ('A generalised linear modelling framework for pairwise and network meta-analysis of randomised controlled trials'; see http://www.nicedsu.org.uk/). Model code is provided in Appendix L.

See additional detail of the methods used for NMAs in Section 2 of the full version of the guideline and in Appendix L.

Grading of Recommendations Assessment, Development and Evaluation (GRADE) Process

The body of evidence identified for each therapy or treatment review question (or part of a review question) was presented in the form of a GRADE evidence profile summarising the quality of the evidence and the findings (pooled relative and absolute effect sizes and associated CIs). Where possible, the body of evidence corresponding to each outcome specified in the review protocol was subjected to quantitative meta-analysis. In such cases, pooled effect sizes were presented as pooled RRs, pooled ORs, or mean differences. A random-effects model was used as default.

Where quantitative meta-analysis could not be undertaken, the range of effect sizes reported in the included studies was presented in a GRADE profile.

GRADE was used to assess the quality of evidence for the selected outcomes as specified in 'The guidelines manual (2012)' (see the "Availability of Companion Documents" field). The type of review question determines the highest level of evidence that may be sought. For issues of therapy or treatment, the highest possible evidence level is a well-conducted systematic review or meta-analysis of randomized control trials (RCTs), or an individual RCT. In the GRADE approach, a body of evidence based on RCTs has an initial quality rating of high, but this may be downgraded to moderate, low or very low if the factors listed above are not addressed adequately. For diagnostic review questions on prognosis, the highest possible level of evidence is a controlled observational study (a cohort study or case–control study), and a body of evidence based on such studies would have an initial quality rating of low, which might be downgraded to very low or upgraded to moderate or high, depending on the factors listed above.

For each review question the highest available level of evidence was sought. Where appropriate, for example, if a systematic review, meta-analysis or RCT was identified to answer a question directly, studies of a weaker design were not considered. Where systematic reviews, meta-analyses and RCTs were not identified, other appropriate experimental or observational studies were sought.

GRADE Profiles for Interventional Evidence

The quality ratings for each study are reported the study's evidence table and are summarised in the footnotes of each GRADE profile. For this guideline, the GDG inserted footnotes to explain the choice made while assessing the quality of evidence for each outcome. These footnotes indicated if the evidence was upgraded a level, downgraded a level or left the evidence level unchanged, and gave the rationale for doing this. See Table 3 in the full version of the guideline.

Modified GRADE for Diagnostic Evidence

GRADE has not been developed for use with diagnostic studies; therefore a modified approach was applied using the GRADE framework.

Cohort studies within the GRADE approach start at the low quality level due to accepted inherent study design limitations. Within a modified approach, where evidence from cohort studies has been deemed to be the most appropriate source of information to answer a given review question, studies start from a presumption of 'high quality'. The same criteria (risk of bias, inconsistency, imprecision and indirectness) were used to downgrade the quality of evidence as detailed in Table 4 in the full version of the guideline.

Modified GRADE for NMAs

The use of GRADE to assess the quality of studies addressing a particular review question for pairwise comparisons of interventions is relatively established. However, the use of GRADE to assess the quality of evidence across a NMA is still a developing methodology. While most criteria for pairwise meta-analyses still apply, it is important to adapt some of the criteria to take into consideration additional factors, such as how each 'link' or pairwise comparison within the network applies to the others. See Table 5 in the full version of the guideline for the rationale for downgrading quality of evidence in NMAs.

Interpreting the Findings

The outcomes prioritised in the review questions and protocols reflect the treatment objectives outlined in each question. The minimum important difference (MID) for both dichotomous and continuous outcomes was decided by looking at appropriate published evidence or under agreement with the GDG following discussion within committee meetings. On the occasion that no published literature on the minimal important difference was identified and the GDG was unable to specify one, a default option was used, for example, in the case of dichotomous outcomes was defined as a relative risk reduction or an increase of 25% or more to be considered clinically important.

For this guideline, the effectiveness of interventions/diagnostic strategies to manage TB has been assessed against a variety of outcomes. The justification for using these outcomes is based on their relevance to people with the condition and the expert consensus opinion of members of the multidisciplinary GDG. When assessing the effectiveness of a particular treatment, information about the effect of that treatment on one or more primary outcomes was sought.

Health Economics

There are 2 parts of the appraisal process. The first step is to assess applicability (that is, the relevance of the study to the specific guideline topic and the NICE reference case); evaluations are categorised according to the criteria in Table 7 of the full version of the guideline. In the second step, only those studies deemed directly or partially applicable are further assessed for limitations (that is, methodological quality); see categorisation criteria in Table 8 of the full version of the guideline.

Where relevant, a summary of the main findings from the systematic search, review and appraisal of economic evidence is presented in an economic evidence profile alongside the clinical evidence.

Original health economic modelling was available to support the GDG's decision making for 3 topics in the 2016 update. The GDG prioritised areas in which they felt that original analysis would be particularly informative, on the grounds of uncertainty and variation in current practice and/or the presence of complex trade-offs between the benefits, harms and costs of various courses of action. The 3 topics that were selected were: diagnosing latent TB (this work was undertaken by external investigators, Warwick Evidence; see section 3.1 in the full version of the guideline), duration of isolation for infectious TB (this work was undertaken by the NICE Internal Clinical Guidelines team; see section of 6.2 in the full version of the guideline) and treatment of latent TB (this work was undertaken by external investigators, Imperial College, London; see section 7.2 in the full version of the guideline).

In questions for which no published evidence was identified and original analysis was not prioritised, the GDG made a qualitative judgement about cost effectiveness by considering potential differences in resource use and cost between the options alongside the results of the review of evidence of clinical effectiveness.

Presentation of Results

Meta-Analyses and Reviews

The results of the meta-analyses were presented in a draft chapter sent to the GDG before each meeting. In the meeting, the findings were presented in evidence tables, excluded studies tables, GRADE profiles with forest plots (where available) and evidence statements on the findings. Statements summarising the GDG's interpretation of statements of the evidence and any extrapolation from the evidence used to form

recommendations were also prepared to ensure transparency in the decision-making process.

Presentation of Results for NMAs

The results of the network meta-analyses were presented in a number of ways.

- Network diagram, showing availability of evidence. These diagrams have the following features:
  - The size of each node is proportional to total number of participants randomised to receive the treatment in question across the evidence-base.
  - The width of connecting lines is proportional to number of trial-level comparisons available.
  - Where possible, arrowheads are added to the connecting lines to indicate direction of effect in direct pairwise data (a > b denotes a is more effective than b) – filled arrowheads show comparisons where one option is significantly superior ($p<0.05$); outlined arrowheads show direction of trend where effect does not reach statistical significance. It has not been possible to add these for some analyses, as it is not straightforward to quantify direct effects with more complex models.
- Plot of the relative effectiveness, including the results of the NMA of each regimen compared with the reference treatment and any direct estimate available for the same comparison.
- Tabulated rank probabilities, giving the probability of each treatment being best (that is, ranked #1) and its median rank with 95% credible interval (CrI). In these outputs, higher ranking always reflect a positive patient outcome (for example: higher rates of disease eradication, lower rates of adverse events, and so on).

Public Health Sections

The public health sections of this guideline were developed in accordance with the methods set out in Methods for the development of NICE public health guidance (third edition) 2012 within the Centre for Clinical Practice process and framework.

The minutes of the GDG provide further detail about the GDG interpretation of the evidence and development of the recommendations.

Service Delivery Section

Critical Appraisal

All studies included in the effectiveness or economic components of the review were critically appraised using relevant checklists from the NICE CPH manual and the NICE Interim methods guide for developing service guidance (February 2013). Critical appraisal was undertaken by one reviewer and checked in detail by a second reviewer for each included study in the effectiveness review. Details of the tools used are provided in Chapter 3 of the service delivery report (see Appendix G7).

Studies or papers used in the case studies were not critically appraised due to the more discursive nature of this component of the review. Rather than present effectiveness data, the aim here was to build descriptive pictures of the way that TB services are organised (in themselves and in relation to wider health services) in each case area.

Data Extraction and Synthesis

Papers identified as being of relevance to case studies were grouped by location. Due to the large volume of information available for this section, much of which overlapped, extraction was not undertaken for each individual paper. Instead, for each location, a case study extraction sheet was prepared, focussing on key audit questions of relevance to the case studies.

Studies included in the effectiveness and economic elements of the review were extracted into evidence tables. Data extraction was conducted by one reviewer and checked in detail by a second reviewer. Data were synthesised narratively, and studies were grouped on the basis of outcome. A further level of synthesis was subsequently undertaken on studies which provided a comparison of one service delivery model/intervention with another service delivery model/intervention, and which provided outcome data that could be linked with the reviews key outcomes: diagnostic delay, treatment completion or contract tracing.

Methods Used to Formulate the Recommendations

Expert Consensus

Informal Consensus

Description of Methods Used to Formulate the Recommendations

Note from the National Guideline Clearinghouse (NGC): This guideline was developed by the Internal Clinical Guidelines Team on behalf of the National Institute for Health and Care Excellence (NICE). See the "Availability of Companion Documents" field for the full version of this guidance and related appendices, including methodology used for previous versions of the guideline.

Clinical Sections

The new clinical sections of the guideline were developed in accordance with the process set out in 'The guidelines manual (2012)' (see the "Availability of Companion Documents" field). There is more information about how NICE clinical guidelines are developed on the NICE Web site. A booklet, 'How NICE clinical guidelines are developed: an overview for stakeholders, the public and the NHS' is available. In instances where the guidelines manual does not provide advice, additional methods are used are described in the full version of the guideline.

Agreeing the Recommendations

For each review question, recommendations for clinical care were derived using, and linked explicitly to, the evidence that supported them. In the first instance, informal consensus methods were used by the Guideline Development Group (GDG) to agree short clinical and, where appropriate, cost effectiveness evidence statements, which were presented alongside the evidence profiles. The 'Linking evidence to recommendations' (LETR) criteria used in moving from evidence to recommendations were:

- Relative value placed on the outcomes considered
- Consideration of the clinical benefits and harms
- Consideration of net health benefits and resource use
- Quality of the evidence
- Other considerations (including equalities issues)

In areas where no substantial clinical research evidence was identified, the GDG considered other evidence-based guidelines and consensus statements or used their collective experience to identify good practice. The health economics justification in areas of the guideline where the use of National Health Service (NHS) resources (interventions) was considered was based on GDG consensus in relation to the likely cost effectiveness implications of the recommendations. The GDG also identified areas where evidence to answer their review questions was lacking and used this information to formulate recommendations for future research.

The wording used in the recommendations in the guideline denotes the certainty with which the recommendations were made. Some recommendations were made with more certainty than others. Recommendations are based on the trade-off between the benefits and harms of an intervention, whilst taking into account the quality of the underpinning evidence.

For all recommendations, it is expected that a discussion will take place with the patients about the risks and benefits of the interventions, and their values and preferences. This discussion should help the patient reach a fully informed decision.

Public Health Sections

The public health sections of this guideline were developed in accordance with the methods set out in Methods for the development of NICE public health guidance (third edition) 2012 within the Centre for Clinical Practice process and framework.

The minutes of the GDG provide further detail about the GDG interpretation of the evidence and development of the recommendations.

Service Delivery Section

Service delivery guidance aims to provide recommendations on:

- What resources need to be available
- How services should be organised and configured
- The processes that need to be followed to ensure the efficient provision of healthcare interventions of proven clinical and cost effectiveness

Recommendations on service delivery were developed following NICE's interim guide for developing service guidance 2014 and using review methods from NICE's methods for the development of public health guidance (2012) with the Centre for Clinical Practice process and framework.

Group Constituency

A group of GDG members and additional co-opted experts were tasked with interpreting the presented evidence and drafting recommendations. This 'Service Delivery' group met on 5 occasions and drafted recommendations on the organisation and management of clinical and public health tuberculosis (TB) services, and subsequently discussed and agreed by the GDG. Any comments suggestions made by the GDG are noted in the relevant LETR tables.

Rating Scheme for the Strength of the Recommendations

Strength of Recommendations

Some recommendations can be made with more certainty than others. The Guideline Development Group (GDG) makes a recommendation based on the trade-off between the benefits and harms of an intervention, taking into account the quality of the underpinning evidence. For some interventions, the GDG is confident that, given the information it has looked at, most patients would choose the intervention. The wording used in the recommendations in this guideline denotes the certainty with which the recommendation is made (the strength of the recommendation).

Interventions That Must (or Must Not) Be Used

The GDG usually uses 'must' or 'must not' only if there is a legal duty to apply the recommendation. Occasionally the GDG uses 'must' (or 'must not') if the consequences of not following the recommendation could be extremely serious or potentially life threatening.

Interventions That Should (or Should Not) Be Used – a 'Strong' Recommendation

The GDG uses 'offer' (and similar words such as 'refer' or 'advise') when confident that, for the vast majority of patients, an intervention will do more good than harm, and be cost effective. Similar forms of words (for example, 'Do not offer…') are used when the GDG is confident that an intervention will not be of benefit for most patients.

Interventions That Could Be Used

The GDG uses 'consider' when confident that an intervention will do more good than harm for most patients, and be cost effective, but other options may be similarly cost effective. The choice of intervention, and whether or not to have the intervention at all, is more likely to depend on the patient's values and preferences than for a strong recommendation, and so the healthcare professional should spend more time considering and discussing the options with the patient.

Recommendation Wording in Guideline Updates

The National Institute for Health and Care Excellence (NICE) began using this approach to denote the strength of recommendations in guidelines that started development after publication of the 2009 version of 'The guidelines manual' (January 2009). This does not apply to any recommendations ending [2006], [2011] and [2012]. In particular, for recommendations labelled [2006] and [2012], the word 'consider' may not necessarily be used to denote the strength of the recommendation.

Cost Analysis

Clinical Sections

Where relevant, a summary of the main findings from the systematic search, review and appraisal of economic evidence is presented in an economic evidence profile alongside the clinical evidence for each question in the full version of the guideline.

Original health economic modelling was available to support the Guideline Development Group's (GDG's) decision making for 3 topics in the 2016 update. The GDG prioritised areas in which they felt that original analysis would be particularly informative, on the grounds of uncertainty and variation in current practice and/or the presence of complex trade-offs between the benefits, harms and costs of various courses of action. The 3 topics that were selected were: diagnosing latent tuberculosis (TB) (this work was undertaken by external investigators, Warwick Evidence; see Section 3.1 in the full version of the guideline), duration of isolation for infectious TB (this work was undertaken by the NICE Internal Clinical Guidelines team; see Section of 6.2 in the full version of the guideline) and treatment of latent TB (this work was undertaken by external investigators, Imperial College, London; see Section 7.2 in the full version of the guideline).

In questions for which no published evidence was identified and original analysis was not prioritised, the GDG made a qualitative judgement about cost effectiveness by considering potential differences in resource use and cost between the options alongside the results of the review of evidence of clinical effectiveness.

TB Service Delivery

Chapter 5 of the evidence review of TB service delivery (see Appendix G7 in the full guideline appendices [see the "Availability of Companion Documents" field]) explores the literature on the economics of service delivery models for the delivery of TB services. The results of the economic review provide evidence of the costs and benefits of several different service delivery interventions/models. However, all of the evidence of specific interventions is limited to one study; two of which were only available in abstract form. All of the studies focussed on individual aspects of TB service delivery. Only one study was a cost-utility analysis and presented economic data in terms of incremental cost effectiveness ratios.

See Appendix G7 for additional details.

Method of Guideline Validation

External Peer Review

Internal Peer Review

Description of Method of Guideline Validation

The guideline was validated through two consultations.

1. The first draft of the guideline (the full guideline and National Institute for Health and Care Excellence [NICE] guideline) were consulted with Stakeholders and comments were considered by the Guideline Development Group (GDG).
2. The final consultation draft of the full guideline, the NICE guideline and the Information for the Public were submitted to stakeholders for final comments.

The final draft was submitted to the Guideline Review Panel for review prior to publication.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of evidence supporting the recommendations is not specifically stated.

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Many cases of tuberculosis (TB) can be prevented by public health measures and when clinical disease does occur, most people can be cured if treated properly.

See the "Trade-off between clinical benefits and harms" sections in the full version of the guideline (see the "Availability of Companion Documents" field) for benefits of specific interventions.

Potential Harms

- Underdiagnosis or overdiagnosis of tuberculosis (TB) (false-negatives and false-positives)
- Adverse effects of TB drug therapy, such as hepatotoxicity. See Table 21 in the full version of the guideline (see the "Availability of Companion Documents" field) for pharmacological considerations for people with human immunodeficiency virus (HIV) who are being treated for tuberculosis.
- Reactions to Bacille Calmette-Guerin (BCG) vaccination
- Steroids have the potential to reduce the inflammatory response and therefore may mitigate against the adverse effects of the

immunopathology. On the other hand, by interfering with the immune response steroids may permit bacilli to continue to multiply, thus slowing or preventing the resolution of the pathology through chemotherapy. There are also concerns that steroids may reduce the effects of antituberculosis drugs, either by interfering with absorption or by pharmacokinetic interactions. In addition, steroids have additional potential effects, reducing the body's own steroid responses from the adrenal glands, osteoporosis, psychosis, upper gastrointestinal ulceration and bleeding, and increasing patients' vulnerability to other bacterial and fungal infections.

See the "Trade-off between clinical benefits and harms" sections in the full version of the guideline for additional discussion of harms of specific interventions.

Contraindications

Contraindications

- Rifampicin is contraindicated in combination with boosted protease inhibitors; co-administration with etravirine therefore is also not recommended.
- The use of some antituberculosis drugs is contraindicated completely in patients with drug-induced liver disease.
- Bacille Calmette-Guerin (BCG) is a live vaccine and as such is contraindicated in a number of situations where the immune system may be compromised, particularly if the person is known or suspected to be human immunodeficiency virus (HIV) positive, because of the risk of generalised BCG infection.

Qualifying Statements

Qualifying Statements

- Healthcare professionals are expected to take National Institute for Health and Care Excellence (NICE) clinical guidelines fully into account when exercising their clinical judgement. However, the guidance does not override the responsibility of healthcare professionals to make decisions appropriate to the circumstances of each patient, in consultation with the patient and/or their guardian or carer.
- For all recommendations, NICE expects that there is discussion with the patient about the risks and benefits of the interventions, and their values and preferences. This discussion aims to help them to reach a fully informed decision (see also 'Patient-centred care' in the full version of the guideline).

Implementation of the Guideline

Description of Implementation Strategy

An implementation strategy was not provided.

Implementation Tools

Clinical Algorithm

Mobile Device Resources

Patient Resources

Resources

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Getting Better

Staying Healthy

IOM Domain

Effectiveness

Patient-centeredness

Identifying Information and Availability

Bibliographic Source(s)

National Institute for Health and Care Excellence (NICE). Tuberculosis. London (UK): National Institute for Health and Care Excellence (NICE); 2016 Jan 13. 177 p. (NICE guideline; no. 33).

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2016 Jan 13

Guideline Developer(s)

National Institute for Health and Care Excellence (NICE) - National Government Agency [Non-U.S.]

Source(s) of Funding

National Institute for Health and Care Excellence (NICE)

Guideline Committee

Guideline Development Group (GDG)

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Financial Disclosures/Conflicts of Interest

For a full list of guideline development group and service delivery group declarations of interest, see Appendix A in the full guideline appendices (see the "Availability of Companion Documents" field).

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: National Collaborating Centre for Chronic Conditions. Tuberculosis. Clinical diagnosis and management of tuberculosis, and measures for its prevention and control. London (UK): National Institute for Health and Clinical Excellence (NICE); 2011 Mar. 64 p. (Clinical guideline; no. 117).

This guideline meets NGC's 2013 (revised) inclusion criteria.

Guideline Availability

Available from the National Institute for Health and Care Excellence (NICE) Web site . Also available for download in ePub and eBook formats from the NICE Web site .

Availability of Companion Documents

The following are available:

- Tuberculosis. Prevention, diagnosis, management and service organisation. Full guideline. London (UK): National Institute for Health and Care Excellence (NICE); 2016 Jan. 551 p. (NICE guideline; no. 33). Available from the National Institute for Health and Care Excellence (NICE) Web site .
- Tuberculosis. Prevention, diagnosis, management and service organisation. Appendices. London (UK): National Institute for Health and Care Excellence (NICE); 2016 Jan. (NICE guideline; no. 33). Available from the NICE Web site .
- Tuberculosis. Baseline assessment. London (UK): National Institute for Health and Care Excellence (NICE); 2016 Jan. (NICE guideline; no. 33). Available from the NICE Web site .
- Tuberculosis. Costing report. London (UK): National Institute for Health and Care Excellence (NICE); 2016 Jan. 18 p. (NICE guideline; no. 33). Available from the NICE Web site .
- Tuberculosis. Costing template. London (UK): National Institute for Health and Care Excellence (NICE); 2016 Jan. various p. (NICE guideline; no. 33). Available from the NICE Web site .
- The guidelines manual 2012. London (UK): National Institute for Health and Care Excellence (NICE); 2012 Nov. Available from the

NICE Web site.

Patient Resources

The following is available:

- Tuberculosis. Information for the public. London (UK): National Institute for Health and Care Excellence (NICE); 2016 Jan. 12 p. Available from the National Institute for Health and Care Excellence (NICE) Web site. Also available for download in eBook and ePub formats from the NICE Web site.

Please note: This patient information is intended to provide health professionals with information to share with their patients to help them better understand their health and their diagnosed disorders. By providing access to this patient information, it is not the intention of NGC to provide specific medical advice for particular patients. Rather we urge patients and their representatives to review this material and then to consult with a licensed health professional for evaluation of treatment options suitable for them as well as for diagnosis and answers to their personal medical questions. This patient information has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline's content.

NGC Status

This NGC summary was completed by ECRI on July 18, 2006. The information was verified by the guideline developer on September 29, 2006. This summary was updated by ECRI Institute on February 27, 2012. This summary was updated again by ECRI Institute on April 12, 2016. This summary was updated by ECRI Institute on June 2, 2016 following the U.S. Food and Drug Administration advisory on opioid pain medicines. This summary was updated by ECRI Institute on October 21, 2016 following the U.S. Food and Drug Administration advisory on opioid pain and cough medicines combined with benzodiazepines.

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